AIR FORCE HEALTH STUDY

FINAL REPORT

An Epidemiologic Investigation of
Health Effects in Air Force Personnel
Following Exposure to Herbicides

2002 Follow-up Examination Results
May 2002 to March 2005

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NOTICE

This report presents the results of the 2002 follow-up examination of the Air Force Health Study, the sixth examination in a series of epidemiologic studies to investigate the health effects in Air Force personnel following exposure to herbicides. The results of the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations were presented in six reports: the Baseline Morbidity Study Results (24 February 1987), the Air Force Health Study First Followup Examination Results (15 July 1987), the Air Force Health Study 1987 Followup Examination Results (16 January 1990), the Air Force Health Study Serum Dioxin Analysis of 1987 Examination Results (7 February 1991), the Air Force Health Study 1992 Followup Examination Results (2 May 1995), and the Air Force Health Study 1997 Follow-up Examination Results (22 February 2000).

Given the relationship of the 2002 follow-up examination to the previous examinations, portions of these documents have been reproduced or paraphrased in this report. In addition, portions of the Air Force Health Study Statistical Plan for the 2002 follow-up examination (20 May 1998) have been used in the development of this report. The purpose of this notice is to acknowledge the authors of these previous study reports and documents.

PREFACE

The current report is the last summarizing the results of physical examinations conducted during the Air Force Health Study that began in 1982. For reasons of consistency, all reports follow the same basic analytical plan. This report is comprehensive and detailed, but limited in that (a) it included only those veterans who attended the final physical examination, (b) it addressed only those risk factors that were thought to be important when the study was designed, and (c) it did not account for potentially important risk factors that were discovered after the analytical plan was set. In addition to these six reports, study results have been summarized in articles published in peer-reviewed scientific journals. Such articles differ from the reports in that they (a) incorporate all participants who attended at least one physical examination, (b) use different methods of analysis, (c) focus on particular health endpoints, and (d) include recently discovered risk factors. The results in the journal articles are often consistent, but sometimes lead to conclusions that differ from the six reports. For example, published articles on diabetes in Ranch Hand veterans revealed an association with dioxin exposure consistent with the current report. Published articles on peripheral neuropathy, memory loss, and cancer, however, revealed associations not discussed in this report.

Many of the analyses in this report show no significant differences in health outcomes in the Ranch Hand group. As noted in Section 1.6.7, the lack of a particular finding does not prove that no association exists and should not lead the reader to conclude that there is no association between herbicide exposure and adverse health. In particular, a recently published analysis showed an increase in cancer risk with increased dioxin body burden in Ranch Hand veterans who spent less than 2 years in Southeast Asia; a stratified analysis was performed because years of service in Southeast Asia was identified as a risk factor for cancer in Comparison veterans. These patterns require that more sophisticated statistical models be used to study cancer in Ranch Hand veterans. Consistent with the protocol, study investigators continue to question the underlying assumptions of all analyses, explore new ways to analyze data, and collaborate with specialists to determine whether exposure to Agent Orange adversely affected the health of Ranch Hand veterans.

In the remaining months of this study, articles submitted to journals, but not accepted for publication by the end of the study, will be released. The National Academy of Sciences is currently considering the disposition of study materials after the study ends on September 30, 2006.

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14. ABSTRACT

This report summarizes results from the Air Force Health Study (AFHS) 2002 follow-up physical examination. The AFHS was undertaken to determine whether adverse health effects attributable to exposure to herbicides existed in veterans of Operation Ranch Hand. The men assigned to Operation Ranch Hand flew aerial herbicide spray missions in Vietnam from 1962 to 1971. A comparison cohort comprised Air Force veterans who served in Southeast Asia during the same time period and who were not involved with spraying herbicides. A total of 1,951 veterans participated in the 2002 physical examination - 777 Ranch Hands & 1,174 Comparisons. Statistical analyses assessed differences between Ranch Hands & Comparisons & associations between health-related endpoints & extrapolated initial dioxin, dioxin category, and dioxin measured in 1987. The study has insufficient statistical power to assess increases in the risk of rare diseases. Consistent with past AFHS reports, current results indicate a significant & clinically meaningful adverse relation between type 2 diabetes & exposure to dioxin.

15. SUBJECT TERMS

Agent Orange, Air Force Health Study, Diabetes, Dioxin, Epidemiologic Investigation, Herbicide Orange, Phenoxy Herbicides, Ranch Hand

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EXECUTIVE SUMMARY – 2002 FOLLOW-UP EXAMINATION REPORT

Purpose

The Air Force launched the Air Force Health Study (AFHS) in 1980 to address concerns of veterans, Congress, and the public regarding the consequences of exposure to Agent Orange and other herbicides sprayed during the Vietnam War. Agent Orange and other phenoxy herbicides were contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin). The purpose of the AFHS was to determine whether adverse health effects exist in Air Force veterans of Operation Ranch Hand, the unit responsible for spraying Agent Orange and other herbicides in Vietnam from 1962 to 1971, and whether those adverse effects can be attributed to the veterans' occupational exposure to Agent Orange or its dioxin contaminant. This report summarizes the results of the 2002 physical examination.

Study Design

This prospective epidemiologic study included assessments of health, mortality, and reproductive outcomes. Members of the Ranch Hand unit were identified by military records. A comparison group comprising Air Force veterans who flew or serviced C-130 aircraft in Southeast Asia (SEA) during the same time period that the Ranch Hand unit was active, but who were not involved with spraying herbicides, also was formed. The health assessment included six physical examinations. Each physical examination included an in-person interview and laboratory measurements of blood and urine.

The baseline examination was conducted in 1982; follow-up examinations were performed in 1985, 1987, 1992, 1997, and 2002. Participation in this study was voluntary and informed consent was obtained at the examination sites. The protocol and conduct of the study was reviewed and approved by the Institutional Review Boards at the sponsoring and participating organizations.

Prior to the baseline examination and after excluding those killed in action (Ranch Hand: n=22, Comparison: n=109), up to 10 Comparisons were matched to each Ranch Hand based on age, race, and military occupation. Each Ranch Hand, and a randomly selected Comparison from those matched to him, were invited to participate in the baseline examination in 1982. In accordance with the protocol, the Comparisons selected for the baseline examination were called Original Comparisons. All Ranch Hands and Original Comparisons were invited to participate in follow-up examinations. If an Original Comparison declined to attend an examination, he was replaced by a Comparison with a similar self-perception of health as the refusing Original Comparison among those matched to the same Ranch Hand; these were termed Replacement Comparisons. A total of 1,951 veterans (777 Ranch Hands, 737 Original Comparisons, and 437 Replacement Comparisons) participated in the 2002 physical examination, representing 74.5 percent, 67.4 percent, and 46.0 percent compliance, respectively. Physical examination findings, laboratory measurements, and disease histories were studied. Study group (Ranch Hand, Comparison) and serum dioxin measurements were used to assess herbicide exposure. The dioxin measurements were conducted by the Centers for Disease Control and Prevention. The majority of dioxin measurements used in the study were accomplished at the 1987 physical examination. These measurements are referred to as 1987 dioxin. Within Ranch Hands, median dioxin varied with occupation, least among officers, greatest among enlisted groundcrew, and intermediate in enlisted flyers.

Statistical Methods

Four statistical models were used to assess the statistical significance of associations between health and herbicide exposure. Model 1 simply contrasted the two groups as exposed (Ranch Hand) and unexposed (Comparison) to herbicides. The contrasts were conducted both overall and by occupational stratum (officer, enlisted flyer, enlisted groundcrew). Model 1 contrasts did not use serum dioxin measurements. Models 2, 3, and 4 used the serum dioxin measurements. The initial dioxin body burdens in Ranch Hands were estimated using a first-order pharmacokinetic model. Model 2 assessed the significance of the relation between health and the estimated initial dioxin in Ranch Hand veterans. To implement Model 3, the Ranch Hand cohort was stratified according to three dioxin exposure categories: background, low, and high. The background category comprised Ranch Hands with 1987 dioxin of 10 parts per trillion (ppt) or less. The remaining Ranch Hands (above 10 ppt) were separated into low and high categories by the median of their estimated initial dioxin levels. Model 3 contrasted each of the three Ranch Hand dioxin exposure categories with Comparisons. Model 4 assessed the significance of the relation between health and 1987 dioxin in Ranch Hand veterans.

Strengths and Weaknesses

Study strengths included record verification of reported health conditions, rigorous quality control, good compliance, long follow-up, and adjustment for confounding factors. The study benefited from a two-tiered management structure based on separate but parallel management and technical teams, an independently appointed and administered Advisory Committee, and periodic review by the National Academy of Sciences.

Study weaknesses included the sample size (which prevented the study of rare diseases), imperfect exposure metrics, and, possibly, incomplete adjustment for confounding factors.

Parameters of the Study and Statistically Significant Findings

More than 300 health-related endpoints in 12 clinical areas were studied. Associations found significant after adjustment for confounders are summarized by clinical area. Interpretations were based on toxicological data, biological plausibility, dose-response relationship, and consistency with results of other epidemiologic studies.

General Health Assessment

Self-perception of health, appearance of illness or distress, relative age, and body mass index were studied. Body mass index was positively associated with 1987 dioxin, possibly reflecting the pharmacokinetics of dioxin elimination. The other measures of general health appeared unrelated to herbicide exposure.

Neoplasia Assessment

During the 2002 interview, each participant was asked whether a doctor had told him that he had cancer. Affirmative responses were confirmed by a medical records review. At each examination, suspicious skin lesions were biopsied and the pathology determined. During the entire follow-up period, AFHS staff made every effort to contact and encourage participants to see their physicians regarding abnormal x-ray

findings, laboratory measurements, and pathology reports. Other than skin biopsies, no invasive procedures were used to detect neoplasms at the physical examination.

With regard to malignancies, a mixed pattern of associations with no suggestion of internal or external consistency was found. For example, the risk of basal cell carcinoma was increased among Ranch Hand officers, but not among enlisted groundcrew, the occupation with the highest median dioxin. Similarly, the risk of basal cell carcinoma was increased in the Ranch Hand low dioxin exposure category, but not in the high category. The risk of all-sites cancer was also increased in the low, but not the high dioxin category. These patterns did not suggest an adverse relation between cancer and herbicide exposure.

Neurology Assessment

The neurology assessment included an evaluation of cranial and peripheral nerve function and an examination of the central nervous system. Associations between dioxin and cranial nerve and central nervous system function did not appear consistent or clinically important. The risk of an abnormal visual field was increased in the Ranch Hand background exposure category, but not the high exposure category. The risk of abnormal balance and coordination increased with initial dioxin, but was not increased in the high exposure category or in any occupational subgroup. The risks of abnormal reaction to pinprick and absent patellar reflex were increased in the high dioxin exposure category, providing some support for a relation between dioxin exposure and peripheral nerve function.

Psychology Assessment

Psychological health was evaluated with subscales of the Symptom Checklist-90-Revised (SCL-90-R) and the Wechsler Memory Scale-Revised (WMS-R). Psychoses, alcohol and drug dependence, anxiety, and other neuroses as determined by a medical records review were also studied. None of these outcome measures was associated with herbicide or dioxin exposure.

Gastrointestinal Assessment

Liver disorders were determined by a medical records review. Laboratory assessments of liver metabolism and function, such as levels of triglycerides, C3 complement, alkaline phosphatase and other liver enzymes, haptoglobin, and prothrombin were also studied. The risk of abnormally high triglycerides was increased among Ranch Hand enlisted groundcrew and among those in the low and high dioxin exposure categories. The risk of abnormally high triglycerides increased with initial dioxin. These results suggested subclinical relation between dioxin and lipid metabolism. None of the other measures in this assessment exhibited a consistent or meaningful association with herbicide or dioxin exposure.

Dermatology Assessment

Chloracne is a skin condition recognized as a consequence of exposure to high levels of dioxin and other cyclic organochlorine compounds. It usually appears without long latency after a short interval of exposure to dioxin and persists for about 2 to 3 years. Primary lesions of chloracne were not expected to persist and be noted upon physical examination in 2002. Chloracne might be suggested if the secondary lesions such as scarring, hyperpigmentation, and depigmentation had been observed in the typical distribution areas of chloracne around eyes, temples, and ears. No evidence of chloracne was found in the Ranch Hand or Comparison group.

The dermatology assessment included the occurrence of self-reported acne and physical examination. The occurrence and duration of acne were reported by the participants at the 2002 physical examination. The frequency and occurrence of reported acne after service in SEA were increased in Ranch Hand enlisted groundcrew, the subgroup with the highest median dioxin levels. The frequency of reported acne since SEA service was increased in the background, low, and high dioxin exposure categories. The frequency of acneiform lesions on physical examination was increased only in the background category. The duration of reported acne after service in SEA increased with 1987 dioxin.

The interpretation of the increased frequency of reported acne after service in SEA in Ranch Hand enlisted groundcrew is uncertain because secondary lesions that were observed revealed no association with herbicide or dioxin exposure.

Cardiovascular Assessment

Cardiac function and history of heart disease were studied. Central cardiac function was assessed by measuring blood pressure, heart sounds, and a resting electrocardiograph. Peripheral vascular function was assessed by the presence or absence of carotid bruits, various pulse-point readings, a resting blood pressure index, measures of intermittent claudication and vascular insufficiency, and a funduscopic examination of small vessels. The lifetime history of essential hypertension, myocardial infarction, and stroke or transient ischemic attack was also studied.

Associations between these measures and herbicide exposure were not consistent or clinically interpretable as adverse. One of the findings, the risk of abnormally high diastolic blood pressure, was increased among Ranch Hand enlisted flyers and among Ranch Hands in the high dioxin exposure category. The risk of abnormally high systolic blood pressure, however, was decreased among Ranch Hands in the low and high categories combined; this risk increased with 1987 dioxin in all Ranch Hands. Overall, cardiovascular health did not appear to be adversely associated with herbicide or dioxin exposure.

Hematology Assessment

Red blood cell counts, white blood cell counts, counts of segmented neutrophils, neutrophilic bands, lymphocytes, monocytes, eosinophils, basophils, hematocrit, platelet count, fibrinogen, erythrocyte sedimentation rate (ESR), and red blood cell morphology were studied.

The mean platelet count was increased among Ranch Hand enlisted flyers. The risk of abnormal red blood cell morphology was increased in Ranch Hand enlisted groundcrew and in Ranch Hands in the low and high dioxin exposure categories. The mean ESR was increased in the low and high dioxin exposure categories. White blood cell count decreased as 1987 dioxin increased. These associations did not suggest an adverse relation between herbicide or dioxin exposure and any hematologic diagnosis. They may, however, suggest the future development of inflammatory disorders and monoclonal gammopathies.

Renal Assessment

The history of renal disease and laboratory measures of renal function were studied. The laboratory measurements included urinary protein, urine specific gravity, serum creatinine, blood urea nitrogen, urinary microalbumin, urinary creatinine, and an index of creatinine clearance. The few associations found did not indicate an adverse relation between renal function and herbicide or dioxin exposure.

Endocrine Assessment

Thyroid disease and type 2 diabetes were studied through physical examination, laboratory measurements, and medical records review. The risk of diabetes requiring insulin control was increased in the Ranch Hand high dioxin category. Fasting insulin and the risk of diabetes requiring insulin control increased and time to diabetes onset decreased with initial dioxin. The risk of diabetes requiring oral hypoglycemic or insulin control increased and time to diabetes onset decreased with 1987 dioxin. The risk of abnormally high hemoglobin A1c increased with 1987 dioxin.

The mean thyroid-stimulating hormone was increased in Ranch Hand officers and in all Ranch Hands. The mean luteinizing hormone, the risk of an abnormally high 2-hour postprandial urinary glucose, and abnormally high free testosterone were increased only in Ranch Hand officers.

The adverse associations between type 2 diabetes and dioxin exposure were consistent with findings at previous physical examinations. In contrast, associations between herbicide or dioxin exposure and measures of thyroid function or gonadotropins did not appear consistent or clinically important.

Immunology Assessment

Red cell surface markers, lymphocytes, quantitative immunoglobulins, and a lupus panel were studied. The risk of antinuclear antibody increased with initial dioxin. An examination of individual antibodies revealed no consistent association with dioxin exposure. Overall, there was no consistent or interpretable association between any measure of immune function and herbicide or dioxin exposure.

Pulmonary Assessment

Pulmonary disease history, including history of asthma, bronchitis, and pneumonia, forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), the FEV_1 to FVC ratio, obstructive abnormality, and loss of vital capacity were studied. The frequency of reported pneumonia was increased in Ranch Hand enlisted flyers. The mean FVC was decreased in the low dioxin exposure category. Considering all pulmonary data, these associations did not suggest an adverse relation between respiratory health and exposure to herbicides or dioxin.

Clinically Significant Findings

Consistent with previous AFHS reports, current results indicate a significant and clinically meaningful adverse relation between type 2 diabetes and exposure to dioxin. The risk of diabetes was associated with 1987 dioxin in Ranch Hands. This increase was supported by an increase in disease severity, a decrease in time to onset, and an increase in fasting glucose and hemoglobin A1c with dioxin in Ranch Hand veterans. Similar patterns were observed in 1987, 1992, and 1997.

Ranch Hand enlisted groundcrew and those in the low and high dioxin exposure categories experienced an increased risk of abnormally high triglycerides. The risk of abnormally high triglycerides also increased with initial dioxin. These results suggest a possibility of a subclinical relation between dioxin and lipid metabolism.

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1   INTRODUCTION

This chapter describes the purpose and background of the Air Force Health Study (AFHS) and provides an overview of the study design and format of this report. In addition, it provides considerations that should be made when interpreting the results provided in this report.

1.1   PURPOSE OF THE REPORT

The subject of this report is the 2002 follow-up examination of the morbidity component of the AFHS. The objective of the morbidity component is to continue the investigation of the possible long-term health effects following exposure to herbicides with specific emphasis on Herbicide Orange, a one-to-one mixture of 2,4-D and 2,4,5-T, contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). In this report, the use of the term "dioxin" refers to TCDD. The principal investigators and the AFHS reports have focused on dioxin for most of the study, as derived from the early peer review groups, review of the literature, and the Ranch Hand Advisory Committee. Model 1, the Ranch Hand versus Comparison contrast, however, does address in a general way the exposure to other herbicides and their components. In addition, dioxin is a biomarker that the study has used as a surrogate to estimate exposure to phenoxy herbicides, described in greater detail in Section 1.6.3 of this chapter. Although there are approximately 75 different congeners of dioxin, TCDD is believed to be the most toxic and the only contaminant of 2,4,5-T.

This report describes the procedures and results of the 2002 follow-up examination. It was written primarily for epidemiologists, clinicians, and biostatisticians. Familiarity with the study protocol and prior mortality and morbidity reports is essential to a full understanding of this 20-year study. The report format has been established to be similar to previous reports so that readers can compare results across study phases. All statistical analyses in this report were prescribed by the Air Force prior to data collection. This report, prepared by Science Applications International Corporation (SAIC), is submitted as partial fulfillment of Air Force Contract No. F41624-01-C-1012.

1.2   BACKGROUND

In January 1962, President John F. Kennedy approved a program of aerial herbicide dissemination for the purpose of defoliation and crop destruction in support of tactical military operations in the Republic of Vietnam (RVN). This program, code-named Operation Ranch Hand, dispersed approximately 19 million gallons of herbicides on an estimated 10 to 20 percent of South Vietnam from 1962 to 1971. The herbicides sprayed were code-named Herbicide Green, Herbicide Pink, Herbicide Purple, Herbicide Orange, Herbicide White, and Herbicide Blue. 2,4,5-T was an active ingredient in Green, Pink, Purple, and Orange, and dioxin was produced as an inadvertent contaminant of 2,4,5-T during the manufacturing process. 2,4-D was an active ingredient in Purple, Orange, and White. Picloram was an active ingredient in White; cacodylic acid was the active ingredient in Blue. Of the 19 million gallons of herbicide dispersed, approximately 11 million gallons were Herbicide Orange, also called Agent Orange, the primary defoliant of the six herbicides used in the program (1, 2). In this report, the term "Agent Orange" will be used.

From the start, Operation Ranch Hand was heavily scrutinized because of the controversial nature of the program and the political sensitivity to charges of chemical warfare contained in enemy propaganda. The concerns were initially based on military, political, and ecological issues, but shifted to the issue of health

in 1970. The primary concern in the controversy over the human health effects of these herbicides was related to dioxin, a component in four of the six herbicides sprayed. The Air Force estimates that 368 pounds of dioxin were released over 6 million acres in South Vietnam (1). Claims of exposure to herbicides, particularly to Agent Orange, and perceived adverse health effects among U.S. military service personnel resulted in substantial controversy and, eventually, a class action litigation. Social concern for the Agent Orange issue continues to be reflected in scientific research, media presentations, congressional hearings, and legal action.

Since 1970, governmental agencies, universities, and industrial firms have funded numerous human and animal studies of dioxin effects. A key scientific issue in these studies was the extent of exposure (e.g., who was exposed and to what extent each individual was exposed). Unfortunately, in many of the human studies, population identification and exposure estimation have been scientifically elusive.

In October 1978, the Air Force Deputy Surgeon General made a commitment to Congress and the White House to conduct a health study on the Operation Ranch Hand population. This population comprised the aviators and ground support crews who disseminated the majority of the defoliants in the RVN. The Surgeon General tasked the U.S. Air Force School of Aerospace Medicine at Brooks Air Force Base, Texas, to develop a study protocol. In 1982, after extensive peer review, the study protocol was published (3) and the epidemiologic study began. The now Brooks City-Base organizations responsible for executing the protocol have been reorganized and renamed several times since 1982. Currently, the Air Force Research Laboratory, Human Effectiveness Directorate, is responsible for the technical aspects of the study, and the Aeronautical Systems Center, Human Systems Program Office, is responsible for program management.

In 1987, when the serum assay became available, the Air Force initiated a collaborative effort with the Centers for Disease Control and Prevention (CDC) to measure the serum dioxin levels in the AFHS population. The results of that effort demonstrated that substantially elevated levels of dioxin could still be found in the serum of some Ranch Hands (4, 5). Studies of serum dioxin levels have suggested that of all the military personnel who served in the RVN, the Ranch Hand cohort was one of the most highly exposed to herbicides. If dioxin caused an adverse health effect, then, based on the principle of dose-response, the Ranch Hands should have manifested more or earlier evidence of adverse health.

1.3   STUDY DESIGN

The purpose of the AFHS is to determine whether adverse health effects relative to a similar but unexposed group of Air Force veterans exist and can be attributed to occupational exposure to Agent Orange. The study, comprising mortality, morbidity, and reproductive outcome components, is based on a matched cohort design in a nonconcurrent prospective setting. A baseline examination and five follow-up examinations over 20 years provide a comprehensive approach to the detection of adverse health effects. Complete details on the design are provided in the study protocol.

For the baseline examination, the population ascertainment process identified 1,264 Ranch Hand personnel who served in Southeast Asia (SEA) between 1962 and 1971. At the beginning of the AFHS, a Comparison group was identified. Comparison veterans flew primarily transport missions in SEA during the same time period that the Ranch Hand unit was active. Their units used C-130 transport planes flown and serviced by crews with similar training and background as those of Ranch Hand veterans. While Ranch Hand veterans spent most of their SEA service in Vietnam, Comparison veterans spent on average less than 30 percent of their SEA service in Vietnam and were stationed mostly in Taiwan, the Philippines, Guam, Japan, and Thailand. These veterans may have been stationed in one but usually in at

least two countries and many had repeated tours of duty in the region. A computerized selection procedure was used to identify Comparisons with similar characteristics to each Ranch Hand veteran. A maximum of 10 Comparisons for each Ranch Hand was selected, matching on age, race, and military occupation (officer-pilot, officer-navigator, officer-other, enlisted flyer, enlisted groundcrew). After personnel records review, an average of eight Comparison subjects were matched to each Ranch Hand.

A replacement strategy was devised to maintain participation of the Comparisons. Noncompliant Comparisons were to be replaced by Comparisons with the same values of the matching variables (age, race, and military occupation in SEA) and the same health perception. In this way, the Replacement Comparisons would serve as surrogates for Comparisons who did not participate. Complete information on the selection and participation of study subjects can be found in Chapter 5, Study Selection and Participation.

1.4 MORTALITY AND MORBIDITY COMPONENTS

The mortality component addresses noncombat mortality from the time of the SEA assignment. A baseline mortality review was conducted in 1982, and the mortality follow-up reports include periodic mortality updates for 20 years. For the baseline mortality review and the first four updates, five individuals were randomly selected from the matched Comparison set for each Ranch Hand for a 1:5 design. After 1987, the design was expanded to include all 19,078 veterans in the Comparison population.

The baseline morbidity component, begun in 1982, reconstructed the medical history of each participant by reviewing and coding past medical records. A cross-sectional element, designed to assess the participant's current state of physical and mental health, was based on comprehensive physical examinations and questionnaires. For the morbidity component of the study, each living Ranch Hand and a random living member of his Comparison set were selected to participate in the examination. The morbidity follow-up examination comprises sequential questionnaires, medical records review, and physical examinations in 1985, 1987, 1992, 1997, and 2002. Participation was voluntary and each participant signed an informed consent form at the examination site.

The baseline morbidity assessment, conducted in 1982, disclosed few differences between the Ranch Hands and Comparisons (6). The sustained commitment to pursue the Agent Orange question to its scientific conclusion was demonstrated by the conduct of the morbidity follow-up examinations. These examinations provided the opportunity to confirm or refute some of the baseline findings and to explore subtle longitudinal changes. In the follow-up examinations, the physical and mental health status of the participants during the time interval since the baseline examination was assessed. The results of the follow-up examinations did not reveal major differences in the health status of Ranch Hands and Comparisons since 1982. There was not sufficient evidence to implicate a relation between herbicide exposure and adverse health in the Ranch Hand group.

For the baseline examination and the 1985 and 1987 follow-up examinations, the major focus of the analyses was to compare the health status of the Ranch Hands (i.e., the exposed cohort) with that of the Comparisons (i.e., the unexposed cohort). Methodology to measure dioxin body burden in blood was not made available until February 1987. During the 1987 physical examination, the Air Force initiated a collaborative study with CDC to measure dioxin levels in the serum of Ranch Hands and Comparisons (4, 5, 7). The measurement of serum dioxin levels led to a statistical evaluation to assess dose-response relations between dioxin and the approximately 300 health endpoints in 12 clinical areas. This was the first large-scale study of dose-response effects based on a direct measurement of dioxin. The statistical

analyses associated with the serum data evaluated the association between a specified health endpoint and dioxin among the Ranch Hands. The analyses also contrasted the health of various categories of Ranch Hands having differing serum dioxin levels with the health of Comparisons having background levels (10 parts per trillion [ppt] or less) of serum dioxin (8). The analysis of dose-response relations based on serum assays provided an important enhancement to the previous AFHS investigations.

In 1992, the fourth examination was initiated. During a 10-month period, data for 12 clinical areas were collected. For the next 2 years, the data were prepared and analyzed, and the 1992 follow-up examination report was written. As in previous reports, the analysis focused on group differences between the Ranch Hand and Comparison cohorts and on the association of each health endpoint with serum dioxin levels. Findings revealed a consistent relation between dioxin and body fat that was initially noted in the analysis of the 1987 examination results. Cholesterol and the cholesterol-to-high-density lipoprotein (HDL) ratio were found to be associated with 1987 serum dioxin levels (9). Evidence for a possible association between glucose intolerance, impaired insulin production, and dioxin levels was revealed. Also revealed was a significant association between selected peripheral pulse abnormalities and dioxin levels, and a significant decrement in self-perceived health status of Ranch Hands. Other health endpoints revealed no consistent patterns within or across clinical areas that were suggestive of an adverse relation between health and herbicide or dioxin exposure.

The fifth examination began in 1997 (10). Data were collected and analyzed for 12 clinical areas. The analysis focused on group differences between the Ranch Hand and Comparison cohorts and on the association of each health endpoint with extrapolated initial and 1987 serum dioxin levels. Diabetes and cardiovascular abnormalities represented the most important dioxin-related health problems seen in the 1997 examination. Consistent with previously reported results, the 1997 follow-up examination data indicated a significant and potentially meaningful adverse relation between serum dioxin levels and diabetes. A significant dose-response relation was found, with Ranch Hands in the high dioxin category exhibiting an increase in diabetes prevalence. As a group, Ranch Hands experienced a statistically significant increase in the prevalence of heart disease (excluding essential hypertension). The prevalence of diagnosed essential hypertension and the percentage of Ranch Hands with electrocardiograph (ECG) findings of prior myocardial infarction increased significantly with initial dioxin. Peripheral pulse abnormalities in 1987 and 1992 increased with 1987 dioxin levels, while 1997 peripheral pulse abnormalities did not. Indices of bilateral peripheral polyneuropathy significantly increased with initial and 1987 dioxin levels. These indices also were increased in the high dioxin category. These findings were new and appeared consistent with polyneuropathies observed in studies of industrial exposure; however, the numbers of affected veterans were small and the clinical importance of the findings was uncertain. There were consistent and significant increases in cholesterol, triglycerides, and the cholesterol-HDL ratio with initial and 1987 dioxin. HDL decreased significantly as dioxin increased. These findings also were observed in 1987 and 1992. Isolated group differences existed, but 1987 dioxin levels were strongly related to increases in hepatic enzymes, such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma glutamyltransferase (GGT) and, as previously noted, cholesterol, triglycerides, and HDL.

The sixth and final examination began in May 2002. As in 1985, 1987, 1992, and 1997, this examination was conducted by SAIC in conjunction with Scripps Clinic and the National Opinion Research Center (NORC). Analysis of data collected at the 2002 follow-up examination was the basis for this report.

1.5   ORGANIZATION OF THE REPORT

This report is organized as follows:

- Chapter 1 (Introduction) provides summary background information on the AFHS and discusses specific technical items and issues that may affect the different clinical area assessments.

- Chapter 2 (Dioxin Assay) describes the procedure used to draw blood for the serum dioxin measurements, the analytical method used to determine the dioxin level from the serum, and the quality control (QC) procedures associated with the serum dioxin data.

- Chapter 3 (Questionnaire Methods) gives an overview of the development and implementation of the participant questionnaires.

- Chapter 4 (Physical Examination Methods) describes the conduct and content of the physical examinations.

- Chapter 5 (Study Selection and Participation) presents the methods by which participants were selected and scheduled. This chapter also presents a discussion of the participant replacement strategy, the factors known or suspected to influence study participation, and sources of potential bias.

- Chapter 6 (Quality Control) provides an overview of the specific quality assurance and QC measures developed and used throughout the 2002 follow-up examination.

- Chapter 7 (Statistical Methods) documents the statistical methods used in the individual clinical area assessments and the statistical procedures and results of the half-life analyses performed by the Air Force.

- Chapter 8 (Covariate Associations with Estimates of Dioxin Exposure) examines the associations between exposure (Ranch Hand, Comparison, and measures of dioxin exposure) and the individual covariates used in the different clinical assessments.

- Chapters 9 through 20 present the results and medical discussions of the statistical analyses of the dependent variables for each clinical area. Each chapter also contains a brief overview of pertinent scientific literature. The 12 clinical chapters are as follows:

  Chapter 9:   General Health Assessment
  Chapter 10: Neoplasia Assessment
  Chapter 11: Neurology Assessment
  Chapter 12: Psychology Assessment
  Chapter 13: Gastrointestinal Assessment
  Chapter 14: Dermatology Assessment
  Chapter 15: Cardiovascular Assessment
  Chapter 16: Hematology Assessment
  Chapter 17: Renal Assessment
  Chapter 18: Endocrinology Assessment
  Chapter 19: Immunology Assessment
  Chapter 20: Pulmonary Assessment

- Chapter 21 (Conclusions) summarizes the findings and medical discussions of the 12 clinical areas.

1.6   INTERPRETIVE CONSIDERATIONS

In interpreting results from any epidemiologic study, no single result should be evaluated in isolation or at face value. Rather, interpretations should be addressed in the context of the overall study design, the data collection procedures, the data analysis methods, dose-response effects, strength of association, temporal relation, biological plausibility, and internal and external consistency. This especially applies to the AFHS. This effort is a large-scale, prospective observational study in which thousands of measurements and diagnoses are made on each participant. Those measurements and diagnoses are subjected to extensive statistical analyses, testing thousands of individual hypotheses. Each positive result should be scrutinized relative to findings in other studies, and relative to the statistical methods used and the medical and biological plausibility of the results. Conversely, the lack of a positive result only denotes that the hypothesis of no association was not rejected. This has a very different conclusion than the possibly incorrect assertion that there is no effect. In addition, no epidemiologic study can establish that there is no effect; i.e., that dioxin is safe (11). Critical considerations in the evaluation of results from this study are reviewed below. Other interpretive considerations, such as adjustments to analyses for known confounders, multiple testing, trends in results within a clinical area, and power limitations, are discussed in greater detail in Chapter 7, Statistical Methods.

1.6.1   Study Design and Modeling Considerations

Biased results will be produced if the assumptions underlying any of the statistical models are violated. Four models were used in this report to analyze the health effects of herbicide exposure in Vietnam. The first model contrasts the exposed population (Ranch Hands) with an unexposed group (Comparisons). The second model evaluates the relation between estimated serum dioxin levels from the time of exposure (i.e., initial dioxin) with each health endpoint. The group contrast model is extended in the third model so that the Ranch Hand group is divided into three categories depending on both 1987 levels and estimated initial levels of serum dioxin, and each category is contrasted with the Comparison group. The fourth model evaluates the association between the dependent variables and lipid-adjusted 1987 dioxin levels. The parameters of these four models are summarized in Table 1-1.

Table 1-1. Parameters of Exposure Assessment Models

Model	Cohort(s)	Subset of Cohort	Exposure Characterized by:	Covariates in Analysis (not including endpoint-specific covariates)
1	Ranch Hands and Comparisons	All participants	Group (Ranch Hands versus Comparisons and military occupation)	--
2	Ranch Hands	Lipid-adjusted 1987 dioxin measurement >10 ppt	Extrapolated initial dioxin	Body mass index at the time of the blood measurement of dioxin
3	Ranch Hands and Comparisons	All participants	Group (Ranch Hands versus Comparisons); Ranch Hands categorized according to 1987 dioxin and estimated initial dioxin levels	Body mass index at the time of the blood measurement of dioxin
4	Ranch Hands	1987 dioxin measurement	Lipid-adjusted 1987 dioxin: (102.6*whole-weight 1987 dioxin/total lipids)	--

As in any epidemiologic study, the group contrast (Ranch Hands versus Comparisons) is susceptible to bias toward the null hypothesis of no exposure effect, because of possible exposure misclassification. It may not be true that all Ranch Hands and no Comparisons were occupationally exposed. Recent dioxin data indicate that 45 percent of the Ranch Hands have only background serum dioxin levels. Either these Ranch Hands were never exposed or their initially elevated serum dioxin levels may have decreased to background levels during the time period between exposure and serum dioxin measurement. The AFHS has no additional data with which to determine whether Ranch Hands currently having background dioxin levels had elevated levels in the past because there was no method of measuring dioxin in blood prior to 1987 and because no blood was collected and saved prior to 1982.

The model analyzing the association between health endpoints and extrapolated initial dioxin levels (Model 2) also is vulnerable to bias because it directly depends on two unvalidated assumptions: (a) that dioxin elimination is by first-order pharmacokinetics, and (b) that all Ranch Hands have the same dioxin half-life (7.6 years) (12). If dioxin elimination is first-order, but some Ranch Hands have a shorter half-life than others do, then there would have been misclassification of initial dioxin levels.

The half-life of dioxin has been found to change significantly with body mass index in 213 Ranch Hand veterans with up to four dioxin measurements, derived from serum drawn in 1982, 1987, 1992, and 1997 (12). The half-life increased significantly with higher levels of obesity. The constant 7.6-year half-life used in this report was an estimate derived without adjustment for body mass index (12). As a partial solution to the observed relation between half-life and obesity, analyses using dioxin or initial dioxin (Models 2 and 3) were adjusted for body mass index at the time of the blood measurement of dioxin (see Chapter 7, Statistical Methods). A study of dioxin elimination in 20 men exposed during the accident in Seveso, Italy, has validated the first-order model (13), which was the basis for the half-life estimate used in this report. Validated models of dioxin elimination adjusted for body mass index or changes in body mass index, however, have not yet been derived.

To account for the possible misclassification of exposure between groups, the third statistical model categorizes Ranch Hands into three levels of exposure: background levels of lipid-adjusted dioxin and low and high levels of estimated initial dioxin. Each Ranch Hand dioxin category is contrasted with all Comparisons. Although this model is less dependent on the accuracy of the initial dioxin estimation procedure than the model using continuous initial dioxin estimates, the classification of the Ranch Hands is subject to bias if the half-life and first-order dioxin elimination assumptions are not true. In addition, the Ranch Hands with background levels of lipid-adjusted serum dioxin may contain both unexposed Ranch Hands and exposed Ranch Hands whose serum dioxin levels have decreased to background levels. This will result in a bias toward the null hypothesis of no dioxin effect on the health endpoint.

The model that analyzes the association between a 1987 dioxin measurement and health endpoints (Model 4) may be less subject to bias than Models 1, 2, and 3; however, recent dioxin levels may not be a good measure of exposure if serum dioxin elimination rates differ among individuals. Serum dioxin levels were extrapolated from 1992 measurements to 1987 for Ranch Hand veterans without serum dioxin levels measured in 1987. Serum dioxin levels also were extrapolated from 1997 measurements to 1987 for Ranch Hand veterans without levels measured in 1987 or 1992. In addition, serum dioxin levels were extrapolated from 2002 measurements to 1987 for Rand Hand veterans without levels measured in 1987, 1992, or 1997. These extrapolations were performed only if the most recent measurement was greater than 10 ppt. Therefore, these 1987 dioxin measurements are subject to bias from a possible violation of the half-life and first-order elimination assumptions that affect the initial dioxin estimates.

1.6.2   Information Bias

Information bias, represented by the over- or under-reporting of disease symptoms, was minimized by verifying all diseases and conditions with medical records. It is possible that conditions in Ranch Hands may be more verifiable because they may have been seen by physicians more often than Comparisons. This would be revealed by group differences in the quantity and content of medical records. Because there is no way to quantify these aspects, this potential source of bias remains unexplored. This bias, if it exists, would affect only the models contrasting Ranch Hands and Comparisons (Models 1 and 3) because Comparison data were not used in Models 2 and 4. Information bias due to errors in the data introduced through data entry or machine error is negligible. All laboratory results were subject to strict QC procedures, historical data were verified completely by medical records review, and medical data were subjected to strict QC standards (see Chapter 6, Quality Control).

1.6.3   The Air Force Exposure Index

In the first three AFHS reports, summarizing results of physical examinations conducted in 1982, 1985, and 1987, the potential relation between health endpoints and herbicide exposure in Ranch Hand veterans was assessed using a calculated estimate of herbicide and dioxin exposure. This was called the Air Force exposure index.

Six different herbicides were used in Vietnam by Operation Ranch Hand to defoliate, by aerial spraying from C-123 aircraft. From 1962 through 1965 small quantities of Agents Purple (2,4-D; 2,4,5-T), Blue (cacodylic acid), Pink (2,4,5-T), and Green (2,4,5-T) were sprayed. From 1965 through 1970 more than 11 million gallons of Agent Orange (2,4-D; 2,4,5-T), and smaller quantities of White (2,4-D; picloram) and Blue were sprayed; from 1970 through 1971 only Agents White and Blue were used for defoliation purposes (14). The Air Force exposure index was calculated from military records to measure the potential exposure of a Ranch Hand to any of four dioxin-containing herbicides: Agents Orange, Purple, Pink, and Green. The index was only an estimate of dioxin exposure because the actual concentration of dioxin in the herbicides varied with type and lot and because exposure varied with individual work habits and duties. The calculation of the index was necessary because direct measures of dioxin exposure were not available at that time. Subsequent to 1987, all outcomes in this study have been assessed with group contrasts and the dioxin body burden measured in serum. The 1987 results were analyzed twice, first using the Air Force exposure index (15), and then using the dioxin body burden as the measure of exposure (8).

The Air Force exposure index for a Ranch Hand was defined as the product of a dioxin weighting factor and the gallons of dioxin-containing herbicides sprayed during his tour divided by the number of men sharing his duties during his tour. This formula was based on the untested assumption that the exposure of an individual decreased as the number of men available increased. The calculation was performed for each month of his tour, and the monthly results were summed to produce a single exposure index for each Ranch Hand veteran. Each veteran was then assigned to a low, medium, or high exposure category depending on his calculated index and the tertiles of the index for his job category (officer-pilot, officer-navigator, officer-nonflying, enlisted flyer, or enlisted groundcrew). Additional details of the calculation are given in Thomas et al. (15).

Both measures, the Air Force exposure index and the serum dioxin measurement, have limitations. The exposure index was approximate in that the number of gallons sprayed was based on the totals across all bases rather than at a specific base. In addition, the assumption that exposure decreased as the number of men available increased may not have been reasonable. Interviews with Ranch Hand groundcrew in 1989 revealed that as the workload increased, more men were added to the job, resulting in more men

becoming exposed rather than each man becoming less exposed. Finally, the spectrum of behaviors, skills, duties, weather-related work stoppages, work surges due to war conditions, and other factors (some known, some unknown) were not included in the calculation. For example, some Ranch Hand groundcrew had direct contact with bulk quantities of herbicide by filling the tanks and servicing the equipment, while others drove trucks or forklifts. The index did not distinguish between these two kinds of exposure patterns. In addition, some Ranch Hands were assigned to administrative duties, which were indicated in their military records. The Air Force exposure index was defined as zero for those assigned to administrative duties.

The serum dioxin measurement is also limited as a measure of exposure. Although the half-life of dioxin is long (7.6 years), pharmacokinetic studies of Ranch Hand veterans suggest that the half-life varies with body fat (12). Thus, some veterans may eliminate dioxin quickly and others more slowly. Variation of the dioxin half-life with body fat contributes to variation in the extrapolated initial dose at the time of exposure. In addition, more than 45 percent of Ranch Hand veterans have background levels, precluding extrapolation. Some of those with background levels may have had elevated levels while in Vietnam, while others may not have been occupationally exposed at all. The exposure status of Ranch Hands with background levels cannot be resolved with available data. Furthermore, no validated model exists to assess the adequacy of the estimated initial dose as an estimate of actual exposure among those with dioxin levels above background in 1987, 1992, 1997, or 2002. Use of serum dioxin measurements as a measure of exposure in Vietnam is further confounded by the other possible sources of dioxin exposure. These sources include industrial exposure and environmental factors, such as burning of plastics and fish consumption.

The correlation between the Air Force exposure index and serum dioxin levels was described in the dioxin analysis of the 1987 physical examination results (8). These correlations reflected the high percentage of veterans who would be misclassified with regard to dioxin level if the Air Force exposure index was assumed as the standard. For example, 77 of 287 (26.8%) Ranch Hand veterans in the high Air Force exposure index category had dioxin levels less than 9 ppt (see Table 3.5 of reference 9).

Despite these limitations, the serum dioxin level appears to be the most appropriate measure of exposure in this study because of the following:

- The authors of this report believed it was the best available assessment of dioxin and herbicide exposure.
- It is a direct measurement of the contaminant.
- It has been accurately measured (16).
- It correlates with reported skin exposure to herbicides among enlisted Ranch Hand veterans (17).
- Its elimination in Ranch Hand veterans has followed a plausible pharmacokinetic pattern (12).
- It has been found to be plausibly associated with health conditions in this study and in other studies (18).

Throughout this report, dioxin levels are used as measures of both exposure to dioxin itself and exposure to dioxin-contaminated herbicides, including Agent Orange. Direct contrasts of Ranch Hand and Comparison veterans (Model 1) address the hypothesis of health effects attributable to any herbicide exposure experienced by Ranch Hand veterans during Operation Ranch Hand. Models involving dioxin measurements address the hypothesis that health effects change with the amount of exposure. Dioxin measurements are used as a measure of exposure to dioxin-contaminated herbicides because it is expected

that as exposure to such herbicides increased, dioxin levels should increase. Therefore, the dioxin measurement serves as a direct biomarker of exposure to dioxin-contaminated herbicides. No other direct measure or estimate of herbicide exposure is available with which to address hypothetical dose-response relations with health. Some indirect measures, such as self-report of skin contact among enlisted groundcrew, or simply being a Ranch Hand enlisted groundcrew member, are valuable alternatives because dioxin measures suggest that enlisted groundcrew experienced the heaviest exposures. Reported skin exposure is not addressed in this report, but enlisted groundcrew status is addressed in Model 1. The use of dioxin as a measure of exposure to dioxin-contaminated herbicides is consistent with the goal of the study, which is to determine whether health effects exist and can be attributed to occupational exposure to Agent Orange (3).

1.6.4   Consistency of Results

All statistically significant findings in this report were subjected to clinical review, ensuring internal consistency throughout the report. In addition, these findings were compared to published results from other studies to ensure external consistency.

1.6.5   Strength of Association

A strong adverse association between exposure and a disease condition, if it exists, would be revealed by an increased relative risk. Some authors have suggested that a statistically significant relative risk greater than 2.0 is cause for concern (19). Statistically significant relative risks less than 2.0 are generally considered to be less important than larger risks because relative risks less than 2.0 can arise more easily because of unrecognized bias or confounding. Relative risks greater than 5.0 are less subject to this concern. The numbers 2.0 and 5.0 are epidemiologic guidelines regarding analyses of association between a dichotomous endpoint (disease, no disease) and exposure (yes, no). No such general guidelines have been formulated regarding the analysis of continuously distributed endpoints (such as cholesterol) versus continuously distributed exposure (such as initial or recent serum dioxin measurements).

Statistical power is also an issue in a study with a population this size. A study with a population of 1,951 lacks power to determine increases in relative risks for rare events (such as soft tissue sarcoma) because such events are unlikely to occur in large numbers in a group this small. While certain occupational toxins have a clear diagnostic pathology (e.g., mesothelioma for asbestos, hepatic angiosarcoma for vinyl chloride) virtually nonexistent in the absence of the toxin, other toxins merely increase the risk of nondiagnostic pathology. For example, the AFHS would likely not discern an increase in the relative risk for a rare tumor that does not have a clear diagnostic pathology. By assessing the pathology observed in association with other known environmental risk factors (e.g., tobacco use, alcohol use), it is sometimes possible to provide a limit in the magnitude of effect missed; however, this study has inherent bounds in detecting modest increases in relative risk for infrequent pathology.

1.6.6   Biological Plausibility

The assessment of biological plausibility requires consideration of a biological mechanism relating the exposure and effect of interest. While a lack of biological credibility or even a contradiction of biological knowledge can lead to the dismissal of a significant result, the failure to perceive a mechanism may reflect only ignorance of the state of nature. On the other hand, it is easy to hypothesize biological mechanisms that relate almost any exposure to almost any disease. Thus, while important, the biological explanation of results must be interpreted with caution. In the AFHS, statistically significant results are

subjected to medical review and comparison with previously published results in order to identify consistent and biologically plausible results.

1.6.7   Interpretation of Nonsignificant Results

In this study, a lack of significant results relating dioxin to a particular disease only means that the study is unable to detect a relation between dioxin and health. This does not imply that a relation may not exist, but that if it does exist, it was not detected. A lack of significant results does not mean that dioxin is safe or that there is no relation between dioxin and health. The AFHS was not designed to establish safety; rather, this study was designed to determine whether a hazard existed for the exposed personnel. Determination of safety would require a study at least 10 times as large, as determined in a 1985 study presenting minimal sample size criteria for proof of safety and hazard in studies of environmental and occupational exposures (11).

1.6.8   Extrapolation to Armed Forces Ground Troops

Extrapolation of the serum dioxin results to the general population of ground troops who served in Vietnam was difficult because Ranch Hand and ground troop exposure situations were very different. Based on serum dioxin testing results obtained by the CDC (5) and others (20), nearly all ground troops tested had current levels of dioxin similar to background levels. Even combat troops who served in herbicide-sprayed areas of Vietnam had current levels similar to those in men who never left the United States (with mean dioxin levels of 4.2 ppt and 4.1 ppt, respectively). There is little scientific basis for an extrapolation of these results to the larger population of Vietnam veterans. We cannot exclude the possibility that a limited number of veterans could have been exposed to levels of dioxin comparable to the Ranch Hand veterans, but because blood or adipose tissue were not collected immediately after their return from Vietnam, the actual exposures of these veterans cannot be known. Others may have received long-term low dose exposure. These possibilities and a multitude of factors, including differential elimination and exposures to other persistent organic pollutants, suggest that existing data do not provide an adequate basis for extrapolation.

1.6.9   Considerations for Summarizing Results

A study of this scope with a multitude of endpoints demands, and at the same time defies, meaningful summary tabulation. Such summaries can be misleading because they ignore correlations between the endpoints, correlations between examination results, and the nonquantifiable medical importance of each endpoint. In fact, many endpoints are correlated (e.g., psychological scales and indices developed from combining multiple variables). In addition, such tabulations combine endpoints that are not medically or biologically comparable. For example, diminished sense of smell may be of less medical importance than the presence of a malignant neoplasm. Nevertheless, the AFHS presents a summary of all statistical results in Appendix G of this report. These summaries, however, can be misleading and must be interpreted carefully—an elementary tally of significant, or nonsignificant, results is not appropriate.

REFERENCES

1. Young, A.L., J.A. Calcagni, C.E. Thalken, and J.W. Tremblay. 1978. The toxicology, environmental fate, and human risk of herbicide orange and its associated dioxin. Technical Report OEHL-TR-78-92, USAF Occupational and Environmental Health Laboratory, Brooks Air Force Base, TX.

2. Buckingham Jr., W.A. 1982. Operation Ranch Hand: The Air Force and herbicides in Southeast Asia, 1961-1971. Office of Air Force History, United States Air Force, Washington, DC.

3. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1982. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Study protocol. NTIS: AD A 122 250. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

4. Centers for Disease Control. 1988. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in Air Force Health study participants—preliminary report. *Morbidity and Mortality Weekly Report* 37:309-24.

5. DeStefano, F., O.J. Devine, W.D. Flanders, J.M. Karon, L.L. Needham, D.G. Patterson, and R.M. Worth. 1988. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in U.S. Army Vietnam-era veterans. *The Journal of the American Medical Association* 260:1249-54.

6. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline morbidity study results. NTIS: AD A 138 340. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

7. Pirkle, J.L., W.H. Wolfe, D.G. Patterson, L.L. Needham, J.E. Michalek, J.C. Miner, M.R. Peterson, and D.L. Phillips. 1989. Estimates of the half life of 2,3,7,8-tetrachlorodibenzo-p-dioxin in Vietnam veterans of Operation Ranch Hand. *Journal of Toxicology and Environmental Health* 27:165-71.

8. Roegner, R.H., W.D. Grubbs, M.B. Lustik, A.S. Brockman, S.C. Henderson, D.E. Williams, W.H. Wolfe, J.E. Michalek, and J.C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

9. Grubbs, W.D., W.H. Wolfe, J.E. Michalek, D.E. Williams, M.B. Lustik, A.S. Brockman, S.C. Henderson, F.R. Burnett, R.G. Land, D.J. Osborne, V.K. Rocconi, M.E. Schreiber, J.C. Miner, G.L. Henriksen, and J.A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1992 followup examination results. NTIS: AD A 304 306, 304 308-316. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

10. Michalek, J.E., B.R. Burnham, H.E. Marden, Jr., J.N. Robinson, V.V. Elequin, J.C. Miner, R.W. Ogershok, W.K. Sneddon, W.D. Grubbs, B.C. Cooper, R.G. Land, V.K. Rocconi, M.E. Yeager, D.E. Williams, and M.E.B. Owens. 2000. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1997 follow-up examination results. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

11. Bross, I.D. 1985. Proof of safety is much more difficult than proof of hazard. *Biometrics* 41:785-93.

12. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57:369-78.

13. Needham, L.L., P.M. Gerthoux, D.G. Patterson, Jr., P. Brambilla, W.E. Turner, C. Beretta, J.L. Pirkle, L. Colombo, E.J. Sampson, P.L. Tramacere, S. Signorini, L. Meazza, V. Carreri, R.J. Jackson, and P. Mocarelli. 1997-98. Serum dioxin levels in Seveso, Italy, population in 1976. *Teratogenesis, Carcinogenesis, and Mutagenesis* 17(4-5):225-40.

14. Institute of Medicine. 2001. Veterans and Agent Orange. Update 2000. National Academy Press. Washington, DC.

15. Thomas, W.F., W.D. Grubbs, T.G. Karrison, M.B. Lustik, R.H. Roegner, D.E. Williams, W.H. Wolfe, J.E. Michalek, J.C. Miner, and R.W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

16. Michalek, J. E., R. C. Tripathi, P. M. Kulkarni, and J. L. Pirkle. 1996. The reliability of the serum dioxin measurement in veterans of Operation Ranch Hand. *Journal of Exposure Analysis and Environmental Epidemiology* 6(3):327-38.

17. Michalek, J.E., W.H. Wolfe, J.C. Miner, T.M. Papa, and J.L. Pirkle. 1995. Indices of TCDD exposure and TCDD body burden in veterans of Operation Ranch Hand. *Journal of Exposure Analysis and Environmental Epidemiology* 5:209-23.

18. Institute of Medicine. 1999. Veterans and Agent Orange. Update 1998. National Academy Press: Washington, DC.

19. Breslow, N.E., and N.E. Day. 1980. Statistical methods in cancer research. International Agency for Research on Cancer: Lyon, France.

20. Kahn, P.C., M. Gochfeld, M. Nygren, M. Hansson, C. Rappe, H. Velez, T. Ghent-Guenther, and W.P. Wilson. 1988. Dioxins and dibenzofurans in blood and adipose tissue of Agent Orange-exposed Vietnam veterans and matched controls. *The Journal of the American Medical Association* 259:1661-7.

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2   THE DIOXIN ASSAY

2.1   PARTICIPANTS SELECTED FOR DIOXIN MEASUREMENT

All participants provided approximately 64 mL of blood at the 2002 physical examination to be possibly used for dioxin testing at a later date. Eleven Ranch Hand participants had never provided blood for dioxin testing previously. An additional Ranch Hand had provided blood in 1987, but a dioxin value could not be obtained from that sample. A total of 85 Comparisons had never provided blood for dioxin testing previously. Nine Comparisons had provided blood for dioxin testing at previous examinations, but a result could not be obtained from the sample. The dioxin value was determined for these 12 Ranch Hands and 94 Comparisons in 2003 and was incorporated into the statistical analysis for this report.

2.2   SAMPLE ACQUISITION

After obtaining informed consent and following a Centers for Disease Control and Prevention (CDC) protocol, approximately 64 mL of blood was drawn from all participants for the serum dioxin assay on the morning of the first day of the 2002 physical examination. The participants were instructed to fast after midnight (water was allowed). Samples were drawn with a 19-gauge needle into six 10-mL red-top tubes and one 4-mL lavender tube supplied by the CDC. After the draw, the six 10-mL red-top tubes were allowed to clot at room temperature for 20 to 30 minutes. The lavender tube contained an anticoagulant that prevented clotting and allowed the extraction of plasma, rather than serum, after centrifugation.

The seven tubes of specimens were spun in a 14.5-cm radius centrifuge for 15 minutes at 3,000 revolutions per minute. Plasma then was transferred with a disposable pipette from the lavender tube to a 1.8-mL nunc vial. The serum from the six 10-mL red-top tubes was then transferred to a CDC-supplied 2-ounce glass jar with a Teflon®-lined screw cap. Serum samples were catalogued and stored at -70 °C until shipment. Specimen containers and materials provided by the CDC were dioxin-free.

Appendix A contains the detailed procedures used by Scripps Clinic for the dioxin blood collection and processing. Frozen samples were packed in dry ice in Styrofoam® boxes and shipped from Scripps Clinic in La Jolla, California, to Brooks City-Base, Texas. Specimens were shipped on Tuesdays and Thursdays, the day after specimen collection. At Brooks City-Base, inventory was taken and the specimens were stored at -70 °C until shipment to the CDC. All samples were coded so that the CDC staff were blinded to the exposure group status (Ranch Hand, Comparison) of each specimen.

2.3   ANALYTICAL METHOD

The serum samples were analyzed for dioxin in groupings consisting of a method blank, three unknown samples, and a quality control (QC) pool sample (1, 2). Cholesterol esters, triglycerides, and high-density lipoprotein cholesterol were determined in duplicate by standard methods. Total phospholipids were determined in duplicate by modifying the Folch et al. procedure (3, 4). Free cholesterol was determined in duplicate by an enzymatic method (5). For each analysis, the mean result of duplicate analyses was used to calculate the concentrations of total lipids using the summation method (6), low-density lipoprotein cholesterol, and very low-density lipoprotein cholesterol (7).

2.4   QUALITY CONTROL

Quality assurance was maintained with matrix-based materials well characterized for dioxin concentration and isotope ratios to ensure that the analytical system was within control limits. The concentration in the QC sample from each analytical run was required to be within established 99-percent confidence limits (8, 9). The unlabeled and carbon-13 labeled internal standard isotope ratios were required to be within 95-percent confidence limits. All analytical runs for the dioxin and lipid measurements were within control limits. No dioxin was detected in the blanks (on-column injection of 100 femtograms from a standard solution produces detectable signals greater than three times the background noise).

2.5   DATA DESCRIPTION

The CDC delivered whole-weight and lipid-adjusted dioxin concentrations to the Air Force, together with the total sample weight, weights of lipid fractions, total lipid weight, detection limit, quantitation limit, and all associated QC information, including results from blank samples. The lipid-adjusted dioxin concentration was calculated using the whole-weight dioxin concentration and the total lipid weight. Details of the calculation are discussed subsequently in this chapter.

The Air Force Health Study (AFHS) dioxin database is a combination of the dioxin assay results from the 1987, 1992, 1997, and 2002 examinations. Results that are usable in the statistical analysis have a result code of "G" (good result) or "GND" (good result, but below the limit of detection). Table 2-1 shows the number of usable serum measurements of dioxin by year. Of the 1,951 fully compliant participants for the 2002 follow-up examination, 1,950 (99.9%) had at least one serum measurement of dioxin determined in the 1987, 1992, 1997, or 2002 examination.

Table 2-1. Number of Dioxin Analyses Performed for the AFHS 2002 Physical Examination Participants

Years of Serum Dioxin Analysis	Ranch Hand	Comparison	Total
1987 Only	277	771	1,048
1992 Only	76	179	255
1997 Only	18	95	113
2002 Only	12	94	106
1987 and 1992	30	35	65
1987 and 1997	146	0	146
1987, 1992, and 1997	218	0	218
Total	777	1,174	1,951

Note: References to 1987 include participants from both the 1987 pilot dioxin study and the 1987 follow-up physical examination.

Participants may have been assayed during any combination of five events: the pilot dioxin study conducted in April 1987 (8), the 1987 follow-up examination (May 1987 to March 1988), the 1992 follow-up examination (May 1992 to March 1993), the 1997 follow-up examination (May 1997 to April 1998), or the 2002 follow-up examination (May 2002 to April 2003). The majority of participants had an assay in 1987 through either the pilot dioxin study or the 1987 follow-up examination. Consequently, 1987 was designated as the reference point for post-Southeast Asia (SEA) serum dioxin levels, termed "current dioxin" in some previous AFHS reports and "1987 dioxin" subsequently in this report and the report on the 1997 follow-up examination.

Each participant with a G or GND dioxin result was given a "reference" dioxin assay result derived from the good result. When a participant had multiple assay results, first priority was given to the 1987 pilot dioxin study results, second priority was given to results derived from serum collected at the 1987 physical examination, third priority was given to the 1992 results, fourth priority was given to the 1997 results, and fifth priority was given to the 2002 results. Figure 2-1 outlines this decision process and shows that the first quantitative result was used. Samples with a good result, but below the limit of quantitation, are denoted by GNQ. Samples where no result was obtained are denoted by NR.

Figure 2-1. Decision Process for Determination of Dioxin Results for Analysis

Of the 1,951 fully compliant participants at the 2002 physical examination, 777 were Ranch Hands and 1,174 were Comparisons. One lipid measurement was not available for a Ranch Hand. A total of 1,950 participants (776 Ranch Hands and 1,174 Comparisons) had quantitative dioxin measurements. Table 2-2 summarizes the sample sizes by exposure group.

Table 2-2. Results from Serum Dioxin Measurements

Summary of Sample Size Reduction	Ranch Hand	Comparison	Total
2002 Follow-up examination	777	1,174	1,951
Less: Lipid measurement not available	(1)	(0)	(1)
2002 Follow-up examination participants with a quantitative dioxin result	776	1,174	1,950

If the 1987 pilot dioxin study or follow-up examination measurement was not used, the 1987 dioxin level was derived for each Ranch Hand in the following manner. If the 1992 measurement was used, the level was extrapolated to 1987 levels when the 1992 dioxin concentration surpassed 10 parts per trillion (ppt). If the 1997 measurement was used, the level was extrapolated to 1987 levels when the 1997 dioxin concentration surpassed 10 ppt. If the 2002 measurement was used, the level was extrapolated to 1987 levels when the 2002 dioxin concentration surpassed 10 ppt. These extrapolated lipid-adjusted dioxin values were calculated using a first-order elimination model with a half-life of 7.6 years (10) and a background level of 4 ppt. Levels at or below 10 ppt were not extrapolated because the first-order elimination model was not considered to be valid at background levels (lipid-adjusted 1987 dioxin levels ≤10 ppt). Dioxin results below the limit of detection were calculated as the limit of detection divided by the square root of 2 (11). Details on the extrapolation method are given in Chapter 7, Statistical Methods. A summary detailing the year the measurement was used and whether the dioxin level was extrapolated to 1987 dioxin levels is provided in Table 2-3 by exposure group.

Table 2-3. Summary of Number of Assays Used for 2002 Follow-up Examination Participant Dioxin Measures

Time of Assay for Dioxin Measurement	Ranch Hand	Comparison	Total
Pilot (1987) Dioxin Study	114	36	150
1987 Follow-up Examination	556	770	1,326
1992 Follow-up Examination	76	179	255
Extrapolated to 1987	[23]	[0]	[23]
Not Extrapolated to 1987	[53]	[179]	[232]
1997 Follow-up Examination	18	95	113
Extrapolated to 1987	[3]	[0]	[3]
Not Extrapolated to 1987	[15]	[95]	[110]
2002 Follow-up Examination	12	94	106
Extrapolated to 1987	[1]	[0]	[1]
Not Extrapolated to 1987	[11]	[94]	[105]
Total	776	1,174	1,950

Note: Numbers in brackets represent subtotals and are not part of the overall total.

2.6 LIPID-ADJUSTED AND WHOLE-WEIGHT 1987 DIOXIN MEASUREMENTS

Serum dioxin is defined as the serum concentration of 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin). It can be expressed as a lipid-adjusted or a whole-weight measurement. The lipid-adjusted dioxin measurement, also called "1987 dioxin body burden," is a derived quantity calculated from the formula

ppt = ppq·102.6/W, where ppt is the lipid-adjusted concentration, ppq (parts per quadrillion) is the actual weight of dioxin in the sample (also known as whole-weight dioxin) in femtograms, 102.6 corrects for the average density of serum, and W is the total lipid weight of the sample (9).

The correlation between the serum lipid-adjusted concentration and adipose tissue lipid-adjusted concentration of dioxin has been observed to be 0.98 in 50 persons from Missouri (12). Using the same data, Patterson et al. calculated the partitioning ratio of dioxin between adipose tissue and serum on a lipid-adjusted basis as 1.09 (95% confidence interval: [0.97,1.21]). On the basis of these data, a one-to-one partitioning ratio of dioxin between lipids in adipose tissue and lipids in serum could not be excluded. Measurements of dioxin in adipose tissue generally have been accepted as representing the body burden concentration of dioxin. The high correlation between serum dioxin levels and adipose tissue dioxin levels in the study by Patterson et al. suggests that serum dioxin is also a valid measurement of dioxin body burden.

Table 2-4 summarizes by military occupation and exposure group the serum lipid-adjusted dioxin results of the 776 Ranch Hands and 1,174 Comparisons who had valid dioxin measurements. For Ranch Hands the median level was greatest for enlisted groundcrew and least for officers.

Table 2-4. Summary of Lipid-adjusted Dioxin Results

Military Occupation	Ranch Hand			Comparison		
	n	Median (ppt)	Range (ppt)	n	Median (ppt)	Range (ppt)
Officer	307	7.26	0.42-35.95	462	3.96	0.42-17.26
Enlisted Flyer	132	16.03	0.42-195.45	185	3.68	0.49-15.77
Enlisted Groundcrew	337	24.03	0.64-617.75	527	3.59	0.42-32.31
Total	776	11.43	0.42-617.75	1,174	3.76	0.42-32.31

Note: ppt = parts per trillion.

Figures 2-2 and 2-3 show the distribution of serum lipid-adjusted dioxin for the 776 Ranch Hands and 1,174 Comparisons, respectively, who had valid dioxin measurements. Figure 2-4 compares distributions of serum lipid-adjusted dioxin concentrations for Ranch Hands and Comparisons on the same scale (ppt). Figure 2-5 compares distributions of the logarithm (base 2) of serum lipid-adjusted dioxin concentrations for Ranch Hands and Comparisons on the same scale.

The Ranch Hand dioxin distribution was shifted to the right of the Comparison distribution as shown by the histograms in Figures 2-2 through 2-5. The Ranch Hand dioxin levels ranged from 0 to 617.75 and the Comparison levels ranged up to 32.31. The distributions were approximately lognormally distributed in each group, as revealed in Figure 2-5 by the approximate bell-shaped histogram of logtransformed (base 2) dioxin levels within each cohort. The approximate lognormal distributions motivated the log transformation of dioxin prior to analysis in Models 2 and 4 (see Chapter 7 for a further description of these models).

Figure 2-2. Relative Frequency Distribution of Lipid-adjusted Dioxin Concentrations for 776 Ranch Hands

Figure 2-3. Relative Frequency Distribution of Lipid-adjusted Dioxin Concentrations for 1,174 Comparisons

Figure 2-4. Relative Frequency Distribution of Lipid-adjusted Dioxin Concentrations

Figure 2-5. Relative Frequency Distribution of the Logarithm (Base 2) of Lipid-adjusted Dioxin Concentrations

2.7   SUMMARY

In summary, serum was collected and archived for all participants at the 2002 follow-up examination at Scripps Clinic, and dioxin levels were determined for 12 Ranch Hands and 94 Comparisons for whom a usable dioxin value had not previously been obtained. The serum was shipped from Scripps Clinic to Brooks City-Base to the CDC according to rigid protocols. The data collected for the 12 Ranch Hands and 94 Comparisons from the 2002 follow-up examination assays were combined with data from the 1987 pilot dioxin study, 1987 follow-up examination, 1992 follow-up examination, and 1997 follow-up examination for use in pharmacokinetic studies and for determining post-SEA dioxin levels. After combining data from this and previous follow-up examinations, 776 of the 777 Ranch Hands (99.9%) and all of the 1,174 Comparisons attending the 2002 follow-up examination had quantitative dioxin assay results.

REFERENCES

1. Patterson, D.G., Jr., J. S. Holler, C.R. Lapeza, Jr., L.R. Alexander, D.F. Groce, R.C. O'Conner, S.J. Smith, J.A. Liddle, and L.L. Needham. 1986. High resolution gas chromatographic/high resolution mass spectrometric analysis of human adipose tissue for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 58:705-13.

2. Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L.R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

3. Beveridge, J., and S. Johnson. 1949. The determination of phospholipid phosphorous. *Canadian Journal* 27E:159-63.

4. Folch, J., M. Lees, and G.H. Sloan-Stanley. 1957. A simple method for the isolation and purification of total lipids from animal tissue. *Journal of Biology and Chemistry* 226:497-509.

5. Cooper, G.R., P.H. Duncan, J.S. Hazelhurst, D.T. Miller, and D.D. Bayse. 1982. Cholesterol, enzymic method. In: Vol. 9, Selected Methods for the Small Clinical Chemistry Laboratory. W. E. Faulkner and S. Meites, eds. American Association for Clinical Chemistry. Washington, DC.

6. Cheek, C.S., and D.F. Wease. 1969. A summation technique for serum total lipids: Comparison of methods. *Clinical Chemistry* 15:102-7.

7. Friedewald, W.T., R.I. Levy, and D.S. Fredrickson. 1972. Estimation of the concentration of low density lipoprotein cholesterol in plasma, with use of the preparative centrifuge. *Clinical Chemistry* 18:499-502.

8. Wolfe, W.H., J.E. Michalek, J.C. Miner, and M.R. Petersen. 1988. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in Air Force Health Study participants. Preliminary report. *Morbidity and Mortality Weekly Report* 37:309-11.

9. Akins, J.R., K. Waldrep, and J.T. Bernert, Jr. 1989. The estimation of total serum lipids by a completely enzymatic "summation" method. *Clinica Chimica Acta* 184:219-26.

10. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57(6):369-78.

11. Hornung, R.W., and D.R. Reed. 1990. Estimation of average concentration in the presence of nondetectable values. *Applied Occupational and Environmental Hygiene* 5(1):46-51.

12. Patterson, D.G., Jr., L.L. Needham, J.L. Pirkle, D.W. Roberts, J. Bagby, W.A. Garrett, J. S. Andrews, Jr., H. Falk, J.T. Bernert, E.J. Sampson, and V.N. Houk. 1988. Correlation between serum and adipose tissue levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in 50 persons from Missouri. *Archives of Environmental Toxicology* 17:139-43.

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3   QUESTIONNAIRE METHODS

This chapter describes the development and implementation of the two participant questionnaires used in the Air Force Health Study (AFHS) 2002 follow-up examination: the 2002-03 Study Subject Health Interval Questionnaire and the 2002-03 Study Subject Baseline Questionnaire. Both questionnaires were formatted and administered by the National Opinion Research Center (NORC), a social science research center at the University of Chicago.

The two 2002 questionnaires were comparable to those used in the baseline examination and the 1985, 1987, 1992, and 1997 follow-up examination efforts. In the 1982 baseline examination, interviews were conducted in the participants' homes. In the 1985 follow-up examinations and for a portion of the 1987 follow-up examination, the baseline interview was conducted for participants new to the AFHS at the participants' homes. The baseline interview was conducted for the remainder of the participants new to the AFHS at the 1987 follow-up examination, as well as participants new to the AFHS at the 1992 and 1997 follow-up examinations, at the physical examination site. In the 1985, 1987, 1992, and 1997 follow-up examinations, the interval interviews were conducted in person at the physical examination site. Administration at the physical examination site proved to be more efficient and subject to better quality control (QC). In all examinations before 1997, the questionnaires were administered in hard copy, which was later edited and keyed into the final SAS[®][1] data set. Since the 1997 follow-up examination, the interview responses have been recorded electronically on laptop computers using a computer-assisted personal interviewing (CAPI) system. This method affords an added measure of QC.

While the interval questionnaire was administered to all participants in the current examination[2], the baseline questionnaire was administered to only those participants who had not previously completed that questionnaire. With the exception of the 1997 translation into the CAPI format, the baseline questionnaire has not changed since 1982. The interval questionnaire was designed to capture the participant's health history in the interval since participation in previous follow-up examinations. In addition, the interval questionnaire elicited general health measures for use by the debriefing physicians.

3.1   QUESTIONNAIRE DEVELOPMENT

An objective of questionnaire development in each follow-up examination has been to maintain, to the maximum extent possible, the question wording, context, and procedures used in the 1982 baseline examination. In addition, the interval questionnaire was often augmented to obtain data on new areas of inquiry. The central task of questionnaire development has been to obtain interval histories on questionnaire items, thereby updating the information provided in previous follow-up examinations. For instance, if a study subject participated in the 1997 follow-up examinations, the 2002 interval questionnaire elicited an interval history for the period from 1997 to the present (i.e., date of interview); however, if the subject last participated in the baseline examination or the 1985 follow-up examination, the 2002 interval questionnaire elicited an interval history from that date through the present.

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[1] SAS and all other SAS Institute, Inc., product and service names are registered trademarks or trademarks of SAS Institute, Inc., in the USA and other countries.

[2] Although all participants in the 2002 follow-up examinations were expected to complete the interval questionnaire, two participants were unable to do so. One participant could not complete the questionnaire due to poor health, and the other participant departed early from the examination for family reasons.

3.1.1 Baseline Questionnaire

The baseline questionnaire used during the 2002 examination was developed in 1982 and the questions have not been changed. The 1982 Study Subject Baseline Questionnaire obtained information on demographics, education, occupation, medical history, study compliance, toxic exposures, and reproductive history. In general, responses to histories and other questions where the response does not change over time were obtained in the baseline questionnaire. Each participant completed the baseline questionnaire the first time he participated in the study.

3.1.2 Interval Questionnaire

All participants were asked questions to update their histories since their last interviews. These data were obtained in the interval questionnaire. While the core content of the interval questionnaire has remained constant since its inception, questions have been added to it over the years to support additional research questions and areas of inquiry. With each introduction of a new question, the question was re-asked at each follow-up examination to provide longitudinal data on this item. For the 1985 follow-up examination, questions on risk factors for skin cancer were added. Other questions pertaining to birth defects, drinking habits and history, smoking habits and history, sleep disorders, and occupational exposure to heavy metals and vibrating power tools were subsequently added, as were one-time questions about facts that do not change, such as ethnicity or experiences during service in Vietnam. These one-time questions were administered only to those participants who had not answered them before.

With the exception of the diet assessment, which was administered in the 1992 follow-up examination but discontinued thereafter, the 2002 interval questionnaire contained all the questions in the 1992-93 Study Subject Health Interval Questionnaire, the Interval Supplement Recording Book, and AFHS Forms 1, 1B, 2A, and 8 (the "self-administered" forms). Copies of the 1992-93 Study Subject Health Interval Questionnaire and the Interval Supplement Recording Book were provided in Appendix B of the 1992 Final Report (1). AFHS Forms 1, 1B, 2A, and 8 are provided in Appendix C of the same report.

The following two questions concerning herbicide exposure were added for the 1997 interval questionnaire:

- What percentage of the missions that you flew as part of the aircrew during the Ranch Hand operation were herbicide spraying missions?

- It has been reported that some Vietnam veterans have intentionally drunk herbicides. Have you ever intentionally drunk herbicides?

In the 2002 interval questionnaire, the first question was asked of only those Ranch Hand flight crew members who had not previously answered it. All participants were asked the second question at either the 1997 or 2002 follow-up examination.

The following five questions were added to the 2002 interval questionnaire:

- How many alcoholic drinks did you have in the 2 weeks before you departed for your trip to La Jolla? Please count a drink of alcohol as one can of beer, one glass of wine, one can or bottle of wine cooler, one cocktail, or one shot of liquor.

- Now, I would like to ask you about your personal relationships. Are you currently married, divorced, widowed, separated, never married, or a member of an unmarried couple?

- Now I'd like to ask you some questions about your current employment. Last week were you working full time, including self-employed or regular volunteer work; working part time, including self-employed or regular volunteer work; with a job, but not at work because of temporary illness, vacation, or strike; unemployed, laid off, or looking for work; retired; in school; keeping house; or other (please specify)?

- Do you have a child under 18 living at home? (Please include your children, grandchildren, stepchildren, foster, or adopted children.)

- Now you will be shown a list of your tours of duty in Southeast Asia during the Vietnam War. We are interested in the possibility that you may have volunteered for or otherwise actively sought any of these tours.

  Our records show your [FIRST] tour was [PRELOADED NAME OF TOUR1]. It started [PRELOADED MONTH, YEAR] and ended [PRELOADED MONTH, YEAR], did you volunteer for this tour of duty, not volunteer for this tour of duty, or do you not know or not remember?

Despite the continual introduction of new questions into the interval questionnaire, the administration actually became less burdensome to participants. The CAPI questionnaire grouped questions topically and avoided asking the same question more than once. Data processing procedures allowed certain information known from previous interviews to be carried forward, thus avoiding asking participants information already collected (e.g., causes of deaths of parents, names of siblings).

The goals in developing the CAPI interval questionnaire for the 2002 follow-up examinations included the following:

1. To replicate the 1997 questionnaire, which encompassed the pre-CAPI interval questionnaires and "self-administered" forms. Questions from the additional forms were inserted throughout the questionnaire into sections covering similar subjects.

2. To print health history responses onsite after the interview for use in participant debriefing. These responses were previously available from the hard-copy self-administered forms.

3. To eliminate item nonresponse.

4. To use "bounded recall" techniques to improve participants' abilities to recall information. A longitudinal questionnaire is dependent on the respondent's ability to remember events and to place those events in time. Even when given a precise starting date, respondents frequently repeat information given earlier, neglect to report new information because they thought they had previously reported it, and otherwise misplace events in time or forget them completely. One method of preventing such errors is through the use of "bounded recall," in which the respondent is reminded of information that he has already reported and asked to provide new information. For the 1992 interview, interviewers worked from a hard-copy information sheet containing summaries of key responses from the previous examination. These responses included date of birth, highest educational degree, military status at the last interview, marital status at the last interview, name of spouse or partner at the last interview, and a cumulative list of all children reported during previous interviews. This practice was replicated online for the 1997 and 2002 questionnaires.

5. To minimize redundancies of items asked of participants and to avoid reminders of previously reported sensitive family history items during their interview. These goals were accomplished by including the items from the self-administered forms in the CAPI questionnaire and by

programming the CAPI questionnaire to skip any sensitive family history items, such as parents or children previously reported as deceased.

6. To replicate, to the maximum extent possible, the 1992 and 1997 variables, names, labels, and formats in the final SAS® data set.

7. To lessen the time burden on the participant for the administration of the questionnaires. By combining the self-administered forms with the interval questionnaire and reducing the redundancy of questions, the participants were able to complete this portion of their examinations in a more timely manner.

8. To increase the spelling quality of responses provided by the participant by encouraging good spelling habits among interviewers and performing spellchecking on verbatim data during data processing.

3.2 INTERVIEWER TRAINING

Shortly before the 2002 follow-up examinations began, NORC's Chicago office staff trained 10 interviewers and 1 field manager to administer the 2002-03 Study Subject Health Interval and Study Subject Baseline questionnaires. Two interviewers had administered questionnaires previously in the 1997 follow-up examination. In addition, the senior site supervisor had worked on the AFHS since the 1992 follow-up examination. The interviewers reported to the Field Manager, who in turn reported to the Data Collection Task Leader in Chicago. The Field Manager observed interviews by each interviewer and presented summaries of these assessments each quarter. The NORC Project Director made quarterly visits to the interviewing site. As part of the training process, the NORC interviewing staff was not informed of the exposure status of any study participant either before or after questionnaire completion.

3.3 DATA COLLECTION

Upon arrival at Scripps Clinic, the participant received a schedule that included the time and place for the interval interview (and, if appropriate, the baseline interview) and was assigned an interviewer. In each personal interview conducted for the AFHS, interviewers were required to ask questions exactly as written, were not allowed to interpret questions or interject personal commentary, and were instructed to probe "don't know" responses at least once. As an added QC measure, the CAPI system did not permit them to skip around among sections of the questionnaire.

During the interviews, participants signed both a consent form to obtain health history information and medical records release forms. If a participant did not have all of the information with him to complete the medical release form during the interview, he was given blank medical records release forms and instructed to mail the completed forms to the Air Force. If the medical records required pertained to his now-adult children and required their signature, he was again given blank medical records release forms and instructed to mail the completed forms to the Air Force. If the participant informed the interviewer that he had brought the relevant records with him, that the records had already been submitted to the AFHS, or that the condition had been diagnosed at Scripps Clinic, the interviewer recorded this and did not ask him to complete the medical release form.

After each interview, interviewers used an onsite printing program that was built into the CAPI system to produce a six- or seven-page form containing items from the questionnaire that were needed for the participant debriefings. These forms were transferred to the participants' folders each day. Each evening, the completed interviews were uploaded via modem to the NORC home office in Chicago. At that time,

new participant data and refinements to the questionnaire software also could be downloaded to the interviewing site.

REFERENCE

1. Grubbs, W.D., W.H. Wolfe, J.E. Michalek, D.E. Williams, M.B. Lustik, A.S. Brockman, S.C. Henderson, F.R. Burnett, R.G. Land, D.J. Osborne, V.K. Rocconi, M.E. Schreiber, J.C. Miner, G.L. Henriksen, and J.A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1992 followup examination results. NTIS: AD A 304 306, 304 308-316. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

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4 PHYSICAL EXAMINATION METHODS

The 2002 Air Force Health Study (AFHS) follow-up examination, which was given to 1,951 invited and scheduled participants at Scripps Clinic in La Jolla, California, included the following:

- Laboratory testing

- Physical examinations

- Psychological testing

- Specialized testing (e.g., nerve conduction velocity testing)

- Medical debriefings.

The Combat Experience Questionnaire and skin, hair, and eye color determinations (components of the 1985 follow-up examination) were administered to all participants who did not attend the 1985, 1987, 1992, or 1997 follow-up examinations.

The Air Force carefully prescribed the details of the above examination elements in the Examiners' Handbook, provided in Appendix B. All physical examination procedures were approved by the Air Force Research Laboratory Institutional Review Board (IRB) at Brooks City-Base and by the Scripps Clinic IRB. Clinical variations were neither desired nor authorized; all proposed examination procedural changes were reviewed in detail by Air Force technical and contractual personnel prior to the start of the examinations. An important objective of the entire physical examination process was to ensure that bias was not created by any procedural change. This objective was carried out successfully.

The requirement to maintain blind examinations was particularly stringent. The clinical staff was prohibited from knowing or seeking information as to the group identity (i.e., Ranch Hand, Comparison) of any participant. At the end of his examination, each participant was asked to note on the critique form whether such information was sought by any member of the clinical or paramedical staff. In 2002, three participants indicated that an examining physician had asked them about specific duties in Southeast Asia (SEA). One of these participants later stated that he had answered erroneously. Another stated that he had not been questioned, but rather had volunteered information in casual conversation. The other participant could not be identified because he chose to remain anonymous. In all known cases, the physician or technician involved was reminded to be more careful in his or her conversations.

4.1 EXAMINATION CONTENT

The examination content, as designed by the Air Force, emphasized detection of medical endpoints suspected of being associated with exposure to phenoxy herbicides, chlorophenols, or dioxin. In each follow-up examination, the Air Force has used findings from the previous examination to refine the current examination.

Table 4-1 shows the general content of the 2002 physical examination and psychological test battery. Table 4-2 displays the complete laboratory test series accomplished at Scripps Clinic and Brooks City-Base. Absolute lymphocytes, immunoglobulin measurements, and lupus panel tests were conducted for all subjects. Cell surface markers were studied on a random sample of approximately 40 percent of the combined cohort due to the complexity of the assay and the expense of the tests (Ranch Hand n=302,

Comparison n=462). Randomization was based on the (randomly assigned) 5-digit case number; those with a case number ending with 0, 3, 6, or 9 were selected.

Table 4-1. Elements of the 2002 Follow-up Physical Examination

Elements	Comments
Chest X Ray	Radiologist
Dermatologic Examination	Dermatologist
Peripheral Vascular Examination using Doppler	Technician; Nicotine Abstinence
Electrocardiogram	Cardiologist; Caffeine and Nicotine Abstinence
General Physical Examination	Internist
Immunologic Studies	40% Random Sample of all participants
Neurological Examination	Neurologist
Patient Debriefing	Internist
Psychological Evaluation:	Psychologist
Symptom Checklist 90-Revised (SCL-90-R)	
Wechsler Memory Scale-Revised (WMS-R)	
Pulmonary Function	Pulmonologist; Nicotine Abstinence
Nerve Conduction Velocity Measurements	Technician

Table 4-2. Laboratory Test Procedures Performed

Chemistry	
2-hour Postprandial Glucose (mg/dL)	Fluorescent Treponemal Antibody – Absorption (FTA-ABS) (confirmatory test for venereal disease research laboratory [VDRL] test for syphilis)
2-hour Postprandial Serum Insulin (μIU/mL)	Gamma Glutamyl Transferase (GGT) (U/L)
Alanine Aminotransferase (ALT) (U/L)	High Density Lipoprotein (HDL) Cholesterol (mg/dL)
Alkaline Phosphatase (U/L)	Human Immunodeficiency Virus (HIV)
Aspartate Aminotransferase (AST) (U/L)	Total Lactate Dehydrogenase (LDH) (U/L)
Blood Urea Nitrogen (BUN) (mg/dL)	Quantitative Fibrinogen (mg/dL)
Cholesterol (mg/dL)	Serum Amylase (U/L)
Creatine Kinase (U/L)	Serum Creatinine (mg/dL)
Direct Bilirubin (mg/dL)	Total Bilirubin (mg/dL)
Fasting Glucose (mg/dL)	Triglycerides (mg/dL)
Fasting Insulin (μIU/mL)	Uric Acid (mg/dL)
Coagulation	
Prothrombin Time (seconds)	
Hematology	
Absolute Bands (thousand/mm^3)	Differential Myelocytes (percent)
Absolute Basophils (thousand/mm^3)	Differential Reactive Lymphocytes (percent)
Absolute Eosinophils (thousand/mm^3)	Differential Segmental Neutrophils (percent)
Absolute Lymphocytes (thousand/mm^3)	Erythrocyte Sedimentation Rate (mm/hr)
Absolute Metamyelocytes (thousand/mm^3)	Hematocrit (percent)
Absolute Monocytes (thousand/mm^3)	Hemoglobin (gm/dL)

Table 4-2. Laboratory Test Procedures Performed (Continued)

Hematology (continued)

Absolute Myelocytes (thousand/mm^3)	Mean Corpuscular Hemoglobin (pg)
Absolute Pelger-Huet-like Cells (thousand/mm^3)	Mean Corpuscular Hemoglobin Concentration (gm/dL)
Absolute Reactive Lymphocytes (thousand/mm^3)	Mean Corpuscular Volume (MCV) (cubic micron)
Absolute Segmental Neutrophils (thousand/mm^3)	Pelger-Huet-like Cells (percent)
Differential Bands (percent)	Platelet Count (thousand/mm^3)
Differential Basophils (percent)	Platelet Observation
Differential Cells Counted	Red Blood Cell (RBC) Count (million/mm^3)
Differential Eosinophils (percent)	RBC Morphology
Differential Lymphocytes (percent)	White Blood Cell (WBC) Count (thousand/mm^3)
Differential Metamyelocytes (percent)	WBC Morphology
Differential Monocytes (percent)	

Immunology

Anti-thyroid Antibody	Hepatitis B Surface Antigen
Hepatitis A Total Antibody	Hepatitis B Surface Antigen Confirmatory
Hepatitis B Core Antibody	Hepatitis C Virus Antibody

Lupus Panel

Anti-mitochondrial Antibody	Anti-smooth Muscle Antibody
Anti-nuclear Antibody	Latex Rheumatoid Factor (IU/mL)
Anti-parietal Cell Antibody	Thyroid Microsomal Antibody

Fecal Studies

Fecal Occult Blood

Protein Profile

α-1-Acid Glycoprotein (mg/dL)	Haptoglobin (mg/dL)
α-1-Antitrypsin (mg/dL)	IgA (mg/dL)
α-2-Macroglobulin (mg/dL)	IgG (mg/dL)
Albumin (g/dL)	IgM (mg/dL)
Apolipoprotein B (mg/dL)	Prealbumin (mg/dL)
C3 Complement (mg/dL)	Transferrin (mg/dL)
C4 Complement (mg/dL)	

Diabetes

C-peptide (ng/mL)	Islet Cell Antibodies
Glutamic Acid Decarboxylase Antibodies	Proinsulin (pmol/L) (tests accomplished by Associates
(Glycated) Hemoglobin A1c (percent)	Regional and University Pathology Lab, Salt Lake City)

Endocrine Radioimmunoassay

Estradiol (pg/mL)	Luteinizing Hormone (mIU/mL)
Follicle-stimulating Hormone (FSH) (mIU/mL)	Prostate-specific Antigen (PSA) (ng/mL)
Free T$_3$ (pg/mL)	Thyroid-stimulating Hormone (TSH) (μIU/mL)
Free T$_4$ (ng/dL)	Total Testosterone (ng/dL)
Free Testosterone (pg/mL)	

T & B Lymphocytes and Subsets (special immunology testing performed on 764 participants)

Absolute CD20+ Cells (B Cells) (per mm^3)	CD20+ Cells (B cells) (percent)
Absolute CD3+ Cells (T Cells) (per mm^3)	CD3+ Cells (T cells) (percent)
Absolute CD4+ Cells (Helper T Cells) (per mm^3)	CD4+ Cells (Helper T Cells) (percent)
Absolute CD3+CD4+ Cells (Helper T Cells) (per mm^3)	CD3+CD4+ Cells (Helper T Cells) (percent)
Absolute CD8+ Cells (Suppressor T Cells) (per mm^3)	CD8+ Cells (Suppressor T Cells) (percent)

Table 4-2. Laboratory Test Procedures Performed (Continued)

T & B Lymphocytes and Subsets (special immunology testing performed on 764 participants) (continued)	
Absolute CD3+CD8+ Cells (Suppressor T Cells) (per mm^3)	CD3+CD8+ Cells (Suppressor T Cells) (percent)
Absolute CD16+56+ Cells (Natural Killer Cells) (per mm^3)	CD45 Total Lymphocytes (Common Leukocyte Antigen) (percent)
Absolute Lymphocytes (per mm^3)	Lymphocytes (percent)
CD16+56+ Cells (Natural Killer Cells) (percent)	

Urinalysis	
Leukocyte Esterase	Urinary Glucose – 2-hour Postprandial (g/dL)
Microalbumin (Quantitative) (mg/dL)	Urinary Glucose – fasting first void (g/dL)
Microalbumin to Creatinine Ratio (μg/mg)	Urinary Ketones (mg/dL)
Microalbumin Screen	Urinary Mucus (per high-powered field)
Urinary Bacteria (per high-powered field)	Urinary Nitrites
Urinary Bilirubin	Urinary pH
Urinary Blood	Urinary Protein (mg/dL)
Urinary Casts (per low-powered field)	Urinary RBC (per high-powered field)
Urinary Clarity	Urinary WBC (per high-powered field)
Urinary Color	Urine Creatinine (mg/dL)
Urinary Comment	Urine Specific Gravity
Urinary Crystals (per high-powered field)	Urobilinogen (mg/dL)
Urinary Epithelial Cells (per high-powered field)	

4.2   QUALITY CONTROL

As in the baseline and 1985, 1987, 1992, and 1997 follow-up examinations, quality control (QC) requirements for both laboratory testing and clinical procedures were extensive. Although details are provided in Chapter 6, the following categories summarize the extent of the emphasis on quality. For laboratory testing, Westgard rules (1_{2s}) were used throughout the examination. Single reagent lots and control standards were used when practical, duplicate specimens were routinely and blindly retested, and testing overlaps were mandatory when test reagent lots were changed.

The Scripps clinical team was instructed on examination procedures to ensure clinician consistency. All physicians were board-certified in their examination area. Nineteen physicians participated in the internal medicine, neurology, and dermatology examinations. In addition, 15 radiologists, 3 pulmonologists, and 4 cardiologists performed tests and interpreted results. To reduce observer variability, turnover in the clinical and paramedical staffs was minimized during the 11 months of examinations. One Scripps Clinic physician served as the Project Medical Director responsible for the scheduling, conduct, and QC of the examinations. All examining physicians reviewed the mark-sense examination forms prior to an examination test. As an added quality assurance (QA) and QC measure, formal meetings were held with the examining physicians and technicians to review the data collection forms. These meetings were held by medical specialty so that the attending staff could review and make comments on their specific forms, as well as reach a consensus on diagnostic techniques and abbreviations. To minimize recording errors, the layout of the form was designed to parallel the flow of the clinical examination. Because data transcription was not permitted, each physician was responsible for filling in the bubbled form. To a large extent, the use of these mark-sense forms and subsequent QC measures was the primary reason for a clean clinical data set. Appendix B includes a complete set of these forms.

Additional QC included the following elements:

- A detailed onsite QC process was employed by Scripps Clinic, Science Applications International Corporation (SAIC), and Air Force monitors and personnel.

- Clinical QA meetings were conducted to detect and correct problems.

- Automated blood pressure recording was performed.

4.3   CONDUCT OF EXAMINATIONS

All examinations, from May 2002 to April 2003, were conducted in accordance with the Examiners' Handbook. Excluding weeks with national holidays, two groups of participants, averaging approximately 24 per group, were examined weekly.

A demanding logistics effort was required to contact, transport, and examine the 1,951 study participants. Pre-examination contact included making telephone calls to recruit participants, determining special requirements (e.g., wheelchair assistance), and arranging transportation. Once scheduling was reasonably firm, the SAIC logistics coordinator sent each participant a detailed information package that included an outline of dietary requirements, a stool occult blood testing kit (Hemoccult®) with instructions for compliance, orientation schedules, important telephone numbers, a request for medical records, and local maps designating examination site dining and recreational facilities.

In addition to a participant orientation meeting held on the evening before the examinations, an informational meeting open to accompanying family members and friends was held on the first morning of examinations. Proctosigmoidoscopy, as well as treadmill tests, were made available to participants for a nominal fee. Accompanying family members also were offered the opportunity to use the clinic facilities at a discounted rate.

Each morning of the examinations, the current group of participants, having fasted and abstained from nicotine and caffeine since midnight the previous evening, was transported to the Scripps Clinic. Alcohol was prohibited from 24 hours before the first day of the examination through the second day of the examination. On the first day, each participant was given an individualized 2- or 3-day schedule outlining his medical, interviewing, and laboratory appointments. The schedule carefully noted the specific required periods of caffeine and nicotine abstinence for generalized periods in relation to electrocardiograph, pulmonary function, and Doppler testing. Although the clinic schedules generally were assigned at random, consideration was given to smokers and diabetics because of the fasting and abstinence restrictions. Figure 4-1 shows a typical 2-day schedule prepared for a participant. This schedule was designed for a smoker in good self-reported health.

As in the previous examinations, schedules with specific directions were provided to aid participants in locating clinic departments, even though for many tests, participants were escorted from the waiting room. Throughout the examination day, time was provided for waiting-room activities (i.e., renewal of past friendships, discussions of experiences in SEA, consumption of refreshments when permitted, and completion of paperwork). On the second day of the examination, a portion of the participants completed testing and examinations and received debriefings from an internist. The remaining participants received their debriefings on the third day.

The SCL-90-R psychological test was self-administered and reviewed by a Scripps Clinic psychologist, while the WMS-R was administered and graded by a Scripps Clinic psychologist (see Table 4-1). If a problem was indicated, the participant was advised of the issue during his medical debriefing. Upon

completion of these debriefings, the participants were asked to complete an examination evaluation form. They were also paid their stipends and reimbursed for travel expenses at this time.

On the first examination day, participants were asked to collect their fasting first urine void of the day at the hotel. Upon their arrival at the clinic, each participant had up to 220 mL of blood collected. Two reclining chairs and four standard blood-draw chairs were used for the blood draws. In previous AFHS examinations, participants who were pilots were concerned about the adverse career effects of fainting during blood draws. To avoid fainting, the Scripps Clinic staff asked each participant if he becomes "light-headed" or faint when having his blood drawn. If a participant responded "yes" or was an active pilot, he was assigned to one of the reclining chairs. These chairs were selected because they could be shifted easily into the Trendelenburg position if a participant felt faint.

Detailed immunology testing (see Table 4-2) was conducted on approximately 40 percent of the participants. These participants were identified by the last digit of their participant study identification number used for previous testing, thus establishing a longitudinal connection between examinations. The immunologic tests were subjected to highly structured QC procedures set forth by the Air Force. An additional blood collection of 5 mL was taken 2 hours after the first blood collection to assess 2-hour postprandial glucose and insulin. At that time, a second urine sample was also collected. Of the 220 mL of blood collected from each participant, the Air Force was provided 35 cc of serum and 10cc of whole blood for archival purposes and for HIV, syphilis (Fluorescent Treponemal Antibody – Absorption (FTA-ABS) – confirmatory test for VDRL test), hepatitis B surface antigen, hepatitis B core antibody, hepatitis C, and hepatitis D testing.

AIR FORCE HEALTH STUDY

Participant Name | ID # | Group #

Day: 1   Monday, August 05, 2002

Start Time	Activity	Wait Location	Instructions
0545	Meet in Hotel Lobby	Lobby	
0600	Bus to Scripps		
0615	Orientation	AFHS Lounge	
0645	Blood Draw 1	AFHS Lounge	Technician will call you.
0800	Doppler Exam	AOP 3 A	Go to 3A Lobby. Do not check in. Tech will call you.
0900	Voucher Submittal	AFHS Lounge	Jim will call you.
0915	Blood Draw 2	AFHS Lounge	Technician will call you.
0930	NORC Interview	AFHS Lounge	Interviewer will call you.
1230	Lunch	Green Hospital	
1315	Physical/Dr. Calabro	AOP 3 A	Go to 3A Lobby. Do not check in. Nurse will call you.
1415	Dermatology	AOP 1 B	Go to 1B Lobby. Do not check in. Nurse will call you.
1500	Psychology Exam	AFHS Lounge	Psychologist will call you.
1630	Bus to Hotel	AOP	

AOP=Anderson Outpatient Pavilion   **Note: 2nd urine collection at blood draw**

ECG- Abstain from caffeine one (1) hour prior to ECG. No nicotine day of ECG until test is completed

DOPPLER- No nicotine day of doppler until test is completed

MT04   Printed on Friday, August 02, 2002   2   0

Figure 4-1. Typical 2-day Clinic Schedule

AIR FORCE HEALTH STUDY

Participant Name

ID # | Group #

Day: 2   Tuesday, August 06, 2002

Start Time	Activity	Wait Location	Instructions
0645	Meet in Hotel Lobby	Lobby	
0700	Bus to Scripps		
0830	ECG/Spirometry	AFHS Lounge	Technician will call you.
0930	Neurology Exam	AOP 3 A	Go to 3A Lobby. Do not check in. Nurse will call you.
1015	Chest X-Ray	Green Hospital 1st floor	Please check in.
1200	Lunch	Green Hospital	
1440	Debrief/Dr. Sargeant	AOP 3 A	Go to 3A Lobby. Do not check in. Nurse will call you.
1500	Exit Interview	AFHS Lounge	You will be called.
1530	Bus to Hotel	AOP	

AOP=Anderson Outpatient Pavilion   **Note: 2nd urine collection at blood draw**

ECG- Abstain from caffeine one (1) hour prior to ECG. No nicotine day of ECG until test is completed

DOPPLER- No nicotine day of doppler until test is completed

MT04   Printed on Friday, August 02, 2002   2   0

Figure 4-1. Typical 2-day Clinic Schedule (Continued)

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5   STUDY SELECTION AND PARTICIPATION

5.1   INTRODUCTION

This chapter reviews the 2002 follow-up examination selection process and the compliance and noncompliance of veterans selected for the Air Force Health Study (AFHS). Refusal rates between Ranch Hands and Comparisons are compared, as are the reasons for refusal. These reasons are examined by age, race, and military rank in an attempt to detect possible differences among refusal rates. According to the study protocol (1), all noncompliant Original Comparisons were to be replaced by Comparisons, matched appropriately according to age, race, military rank, and self-reported health status. This chapter assesses the adherence to the replacement strategy as defined in the protocol, and compares the health status of noncompliant Original Comparisons with their Replacement Comparisons. Differences in perception of health are evaluated according to group, age, race, military rank, and 2002 compliance status. Self-reported health status is compared among fully compliant study participants. Because perception of health may differ between Ranch Hands and Comparisons, medication use and work loss are compared as possible surrogate measures of actual health status.

Throughout this chapter, several terms are used to describe veterans who did not participate in the 2002 follow-up examination. These terms include "passive refusal," "hostile refusal," and "final refusal." An individual who communicated a desire not to have any contact with or from the AFHS under any circumstances was classified as a "hostile refusal." Veterans who were classified as hostile refusals in the past were not invited to the 2002 examination (see Section 5.5.2.2). A veteran was classified a "passive refusal" if he was scheduled for a physical examination but twice cancelled the appointment or failed to appear for it. He was also classified a passive refusal if he was unreachable by telephone because of a "gatekeeper" (see Section 5.4.1) or if he failed to respond to correspondence. A veteran who was determined to be a hostile refusal or refused to participate twice was classified as a "final refusal." Veterans who could not attend due to one of the following reasons and their problem could not be resolved were also classified as a "final refusal:"

- Health reasons

- No interest or no time

- Job commitment

- Travel distance, family concerns

- Dissatisfaction with U.S. Air Force or U.S. Government

- Confidentiality, adverse impact on career

- Financial hardship

- Dissatisfaction with AFHS

- Fear of physical exam

- Dissatisfied with previous exams

- Other.

5.2 FACTORS KNOWN OR SUSPECTED TO INFLUENCE STUDY PARTICIPATION

A multitude of factors may influence study participation. These may be classified broadly as health, logistics, demographic, operational, or publicity factors. For example, health factors are thought to include self-perception of health (compared to others of the same age), as well as demonstrable health indicators, such as medication use and workdays lost due to illness or injury. Logistics factors include no time or interest, reluctance to spend time away from family or job, distance to the examination site, confidentiality, or financial hardship. Demographic factors include flying status, age, race, or military duty status (active, retired, separated). Operational factors include any aspect of study operation that may cause differential compliance, such as differential treatment of Ranch Hands and Comparisons during scheduling, physical examination, interview, or debriefing. Publicity factors are related to national attitudes and media presentations regarding the Agent Orange issue, the Vietnam War, veterans' health care, or health care in general. In addition, these considerations may influence Ranch Hands differently than Comparisons.

The issues involved in deciding whether to volunteer for this study are complex, making statistical assessment of compliance bias difficult and necessarily crude in that many of the factors contributing to self-selection cannot be measured directly. Compliance bias was investigated at the 2002 follow-up examination with respect to self-perception of health, medication use, and work loss. Medication use and days lost from work due to illness or injury were obtained from questionnaire and physical examination data and, therefore, were available only for fully compliant participants. In 2002, as in 1992 and 1997, no partial compliance (defined as compliant to the questionnaire and noncompliant to the physical examination) occurred because both the physical examination and the questionnaire were administered at the examination site.

5.3 REPLACEMENT PROTOCOL

During the design phase of the AFHS, the authors of the study protocol anticipated that a loss of participants between follow-up examinations would pose the greatest threat to study validity. In particular, they expected differential compliance, with relatively more Ranch Hands choosing to return to the study than Comparisons and with health differences of unknown character between noncompliant Ranch Hands and noncompliant Comparisons. To partially correct the situation, the study design specified that noncompliant Comparisons would be replaced by Comparisons with the same values of the matching variables (age, race, and military occupation at the baseline examination) and the same current health perception. Military occupation was stratified into the following five categories: (1) flying officer—pilot, (2) flying officer—nonpilot, (3) nonflying officer, (4) flying enlisted, and (5) nonflying enlisted (also referred to as enlisted groundcrew). In this way, the Replacement Comparisons would serve as surrogates for Comparisons who refused to participate. This method of replacement would tend to reduce bias resulting from refusal in the Comparison group and would maintain group size. No corresponding strategy for the Ranch Hands was possible because all living Ranch Hands had been identified and invited to participate.

The first Comparison in each randomized matched set who was asked to participate in the baseline questionnaire and physical examination was identified as the Original Comparison for his respective Ranch Hand (in accordance with the study protocol). If the Original Comparison was noncompliant, a "Replacement" Comparison was invited in his place. Noncompliance was determined if any of the following three conditions were met:

1. The Comparison refused to participate.

2. The Comparison was partially compliant (completed the baseline questionnaire but did not complete the baseline physical examination).

3. The Comparison was unlocatable.

Replacement Comparisons were identified as such in the database to satisfy the study protocol requirement that they be matched with the refusing Original Comparisons (also known as refusals) based on self-reported health (excellent, good, fair, or poor). Of course, in the case of an unlocatable Original Comparison, matching with regard to self-reported health was not possible. Original Comparisons who were partially compliant for previous AFHS follow-up examinations were replaced, but deceased Original Comparisons were not. Replacement Comparisons, who like the Original Comparison were matched by age, race, military rank, and military occupation to a Ranch Hand veteran, were selected from a set of up to nine additional candidate Comparisons.

Health matching of replacements was not used during the baseline examination, but was implemented during the 1985, 1987, 1992, 1997, and 2002 follow-up examinations. During the 1985 examination, a telephone questionnaire was administered to refusals and their potential replacements. This questionnaire served as the basis for health matching required by the study protocol, and assessed self-perception of health, days lost from work due to illness, and medication use. Although the study protocol is not explicit on this point, it implies that the decision to include or exclude the replacements from the study should be based only on this health contrast. At the 1987 follow-up examination, instead of using a telephone questionnaire, refusals were asked during the scheduling process for their self-perception of health. During the 1992, 1997, and 2002 follow-up examinations, schedulers requested a current perception of health from all potential participants (compared to others their age) contacted by telephone. Self-perception of health was used in the replacement strategy (described subsequently in Section 5.4.2) to address the possibility that Replacement Comparisons might differ from the noncompliant Original Comparisons they replaced with regard to health, which might bias the study either toward or against the null hypothesis of no difference in health between Ranch Hands and Comparisons.

The complete algorithm for replacing Comparisons is presented as a flowchart in Appendix C for reference purposes.

5.4   2002 FOLLOW-UP SCHEDULING AND REPLACEMENT OPERATION

5.4.1   Scheduling Strategy

The scheduling process included the following three objectives:

1. Maximizing participation rates

2. Ensuring that Ranch Hands and Comparisons were recruited using consistent procedures and amount of effort

3. Ensuring that, whenever possible, each Ranch Hand had at least one compliant Comparison who was matched with that Ranch Hand on age, race, and military occupation.

These objectives led to a set of conflicting priorities: maximizing participation rates meant giving each potential participant every opportunity and encouragement to participate, without being so persistent as to lose the cooperation of somewhat ambivalent veterans. This careful approach had to be balanced against the need to quickly identify noncompliant Comparisons. Until these noncompliant Comparisons were removed from the scheduling process, they could not be replaced. In general, prospective participants were contacted for scheduling in random order; however, priority was given to certain potential participants who needed to be contacted early in the scheduling period. These included the following:

- Veterans residing overseas, because they would be more difficult to contact and require advance time to make travel arrangements

- Passive refusals or "no-shows" for previous physical examinations.

During the first 2 months of scheduling, an attempt was made to contact all veterans invited to previous examinations who were not categorized as hostile. In addition, all previously invited veterans were sent a refrigerator magnet that stated the date that scheduling would begin and the toll-free number of the scheduling operation.

Although every reasonable attempt was made to contact eligible veterans, accommodate unusual schedules, and convert refusals, experience in past examinations had shown that certain types of potential participants ultimately would not schedule appointments. To continue with the replacement of Comparisons, these cases needed to be closed early. Therefore, the following rules were observed to limit the number of calls to certain types of individuals who were not likely to participate:

- An individual classified as hostile to the study in previous follow-up examinations was not contacted in 2002.

- An individual who was extremely hostile in his refusal to initial scheduling contacts was coded as a final refusal.

- If the scheduler did not get an answer on the telephone after eight attempts, a certified letter was sent to that individual. If there was direct evidence that the individual appeared at the post office to claim the letter, but did not contact the scheduling office, he was considered a passive refusal.

- An individual who broke an examination appointment and did not attempt to reschedule ("passive refusal") was considered a final refusal.

- An individual who equivocated about attending the physical examinations twice during the first two contacts was considered a final refusal.

Some potential participants were particularly difficult to reach because of the presence of a "gatekeeper" who did not allow the schedulers to speak directly to the potential participant. A potential participant was designated as a final passive refusal after a minimum of three contacts with a gatekeeper and failure to reach the participant by other means. These contact methods included varying calling times, leaving messages, or sending a certified letter. Up to eight gatekeeper contacts were allowed if the scheduling supervisor decided additional attempts were still warranted (e.g., if an individual had previously scheduled and canceled or if it seemed reasonable that he might reschedule). After these gatekeeper contacts had been exhausted, the individuals were designated as final passive refusals and, if eligible for replacement, replaced. Potential participants who were designated as final refusals at any stage in the scheduling process were provided with the toll-free number for the study and allowed to volunteer to participate at any time, even if a Replacement Comparison had been invited to participate.

Figure 5-1 plots the percentage of persons completing the 2002 follow-up examination by calendar date for Ranch Hands, Original Comparisons, Replacement Comparisons, and all Comparisons. These patterns are similar to those seen at previous follow-up examinations and reflect the study protocol specification that scheduling be random with respect to group. Completion rates are similar between Ranch Hands and Original Comparisons. Replacement Comparisons completed the physical examinations later in the scheduling process, as expected, because new Replacement Comparisons were not recruited until an Original Comparison had refused.

5.4.2   Replacement Strategy

All Comparisons who had participated or had been invited to participate in the baseline, 1985, 1987, 1992, or 1997 follow-up examinations were invited to participate in the 2002 examination. If no previously invited Comparisons for a particular Ranch Hand agreed to participate in 2002, schedulers attempted to recruit a replacement. These replacements were selected from a set of up to nine candidate Comparisons, matched by age, race, military rank, and military occupation, whose self-reported health status in 2002 matched that of the noncompliant Original Comparison for a given Ranch Hand. Health status was recorded in four categories: excellent, good, fair, or poor. If a willing health-matched participant was not found in the matched set, self-reported perceptions of health status were dichotomized into "excellent or good" and "fair or poor" categories and these dichotomized health statuses were matched. If this second method for identifying a suitable replacement failed, no replacement was made. There were two exceptions to the replacement strategy. First, the study protocol required that the noncompliant Original Comparisons report their health status during the scheduling effort so that they could be used to recruit Replacement Comparisons with the same health status. On occasion, Original Comparisons refused to speak with the scheduler or respond to questions. In these cases, a Replacement Comparison for the Original Comparison was recruited in the order in which he was listed in the randomized matched set. This strategy also was used for unlocatable Original Comparisons and hostile Original Comparison refusals. Second, as specified in the study protocol, no replacement was made if all formerly invited Comparisons in a matched set were deceased.

5.5   COMPLIANCE

Of the 1,043 eligible Ranch Hands, 777 (74.5%) participated in the 2002 follow-up examination, while 737 (67.4%) of the 1,093 eligible Original Comparisons participated. Of the 951 Replacement Comparisons eligible for the 2002 follow-up examination, 437 (46.0%) chose to attend the examination. Table 5-1 provides compliance counts for Ranch Hands, all Comparisons as a group, and Original and Replacement Comparisons. Appendix C contains tables that describe these counts by compliance at the baseline examination. Table C-1 provides counts for the Ranch Hands. Table C-2 summarizes total Comparison counts. Table C-3 provides Original Comparison counts and Table C-4 lists Replacement Comparison counts.

In Table 5-1 and Appendix C, the "New to Study" rows include potential Replacement Comparisons who were found to be deceased when contact was attempted. The same deceased potential replacements are then accounted for in the rows marked "Deceased." Undefined categories are indicated by dashes. For example, in Table 5-1, dashes are shown for Ranch Hands and Original Comparisons for the row designated as "No Health Match." As described in Section 5.4.2, attempts were made to find a Replacement Comparison if the Original Comparison did not attend. Thus, health matching is applicable for Replacement Comparisons only and not for Original Comparisons and Ranch Hands.

Figure 5-1. Cumulative Percentage of Participants Who Completed the Physical Examination (by Calendar Date)

Table 5-1. Compliance by Group and Examination Year

Time Period	Disposition	Group Ranch Hand	All Comparisons	Original Comparisons	Replacement Comparisons
Baseline		***1,209***	***1,666***	***1,235***	***431***
1985 Examination	***Eligible***	***1,209***	***1,666***	***1,235***	***431***
Between Baseline and 1985	New to Study	9	73	17	56
Examinations	Deceased	(19)	(26)	(21)	(5)
	Remaining Eligible	***1,199***	***1,713***	***1,231***	***482***
	Unlocatable	(39)	(65)	(48)	(17)
	Refused	(133)	(325)	(219)	(106)
	Partially Compliant	(10)	(31)	(10)	(21)
	Fully Compliant	***1,017***	***1,292***	***954***	***338***
1987 Examination	***Eligible***	***1,199***	***1,713***	***1,231***	***482***
Between 1985 and 1987	New to Study	4	33	4	29
Examinations	Deceased	(15)	(16)	(13)	(3)
	Remaining Eligible	***1,188***	***1,730***	***1,222***	***508***
	Unlocatable	(20)	(47)	(31)	(16)
	Refused	(171)	(358)	(242)	(116)
	Partially Compliant	(1)	(27)	(11)	(16)
	Fully Compliant	***996***	***1,298***	***938***	***360***
1992 Examination	***Eligible***	***1,188***	***1,730***	***1,222***	***508***
Between 1987 and 1992	New to Study	(0)	83	2	81
Examinations	Deceased	(39)	(52)	(33)	(19)
	Remaining Eligible	***1,149***	***1,761***	***1,191***	***570***
	Unlocatable	(12)	(56)	(15)	(41)
	No Health Match	--	(11)	--	(11)
	Refused	(184)	(414)	(264)	(150)
	Fully Compliant	***953***	***1,280***	***912***	***368***
1997 Examination	***Eligible***	***1,149***	***1,761***	***1,191***	***570***
Between 1992 and 1997	New to Study	(0)	236	2	234
Examinations	No Health Match in 1992	--	(11)	--	(11)
	Deceased	(47)	(66)	(42)	(24)
	Remaining Eligible	***1,102***	***1,920***	***1,151***	***769***
	Unlocatable	(4)	(30)	(10)	(20)
	No Health Match	--	(91)	--	(91)
	Refused	(227)	(548)	(302)	(246)
	Not Contacted	(1)	(0)	(0)	(0)
	Fully Compliant	***870***	***1,251***	***839***	***412***
2002 Examination	***Eligible***	***1,102***	***1,920***	***1,151***	***769***
Between 1997 and 2002	New to Study	1	318	1	317
Examinations	No Health Match in 1997	--	(91)	--	(91)
	Deceased	(58)	(100)	(57)	(43)
	Discovered to be Ineligible	(2)	(3)	(2)	(1)
	Remaining Eligible	***1,043***	***2,044***	***1,093***	***951***
	Unlocatable	(3)	(32)	(7)	(25)
	No Health Match	--	(60)	--	(60)
	Refused	(262)	(778)	(349)	(429)
	Not Contacted	(1)	(0)	(0)	(0)
	Fully Compliant	***777***	***1,174***	***737***	***437***

Table 5-2 describes the newly compliant participants in terms of their compliance at previous examinations. Four Ranch Hands, 1 Original Comparison, and 71 Replacement Comparisons were fully compliant and examined for the first time at the 2002 follow-up examination. Of these, one Ranch Hand and 56 Replacement Comparisons had not been invited previously to participate. This new Ranch Hand had not been listed as a member of the Ranch Hand operation for previous examinations but made contact with personnel at Brooks City-Base and was verified to be a Ranch Hand. Three Ranch Hands, 1 Original Comparison, and 15 Replacement Comparisons had been previously invited and had refused to participate in one or more previous examinations.

Table 5-2. Participants Newly Compliant in 2002 and Their Previous Compliance Pattern

Compliance Pattern						Comparisons			
						Ranch Hand	Original	Replace-ment	Total
Baseline	1985	1987	1992	1997	2002				
Partial	Partial	Refused	Refused	Refused	Compliant	1	0	0	1
Partial	Refused	Refused	Refused	Refused	Compliant	1	1	0	2
Partial	Unlocated	Unlocated	Refused	Refused	Compliant	1	0	0	1
	Partial	Refused	Refused	Unlocated	Compliant	0	0	1	1
			Unlocated	Refused	Compliant	0	0	1	1
				No Health Match	Compliant	0	0	5	5
				Refused	Compliant	0	0	8	8
					Newly Compliant	1	0	56	57
					Total	4	1	71	76

5.5.1 Corrections to Previously Reported Study Compliance Totals

Some changes were made to the historical cell counts shown in Table 5-1 (and the tables in Appendix C) so that they now differ from compliance tables presented during previous examinations (in particular, Table 5-1 and Appendix Tables C-1 through C-4 of the 1997 follow-up examination report). In addition, some circumstances regarding new and ineligible Ranch Hands for the 2002 follow-up examination occurred. The differences from previous tables and an explanation of the new and ineligible Ranch Hands are described below.

1. One Ranch Hand and one Original Comparison were reclassified from "Refused" to "Partially Compliant" at the 1985 follow-up examination. These veterans were discovered to have completed a questionnaire, but not the physical examination, in 1985. This change affects Tables 5-1, C-2, and C-3.

2. One Replacement Comparison was thought to be deceased at the 1997 follow-up examination, but was later discovered to be alive, but unlocatable, for the 1997 follow-up examination. This veteran was fully compliant for the 2002 follow-up examination. This change affects the "Deceased" and "Unlocatable" rows for the 1997 follow-up examination in Table 5-1, C-2, and C-4.

3. One Ranch Hand was thought to be deceased for the 1997 follow-up examination, but his death could not be confirmed in a subsequent review of his records after the 2002 follow-up examination had been completed. Additional attempts to contact him or clarify his status after the 2002 follow-up examination have been unsuccessful. Although this veteran may be deceased, his classification for the 1997 and 2002 follow-up examinations has been changed from "Deceased" to "Not Contacted" because of the lack of verification of his death. This change affects Tables 5-1 and C-1.

4. One additional Ranch Hand was discovered during the 2002 follow-up examination. This new Ranch Hand had not been listed as a member of the Ranch Hand operation for previous examinations but made contact with personnel at Brooks City-Base and was verified to be a Ranch Hand. This new Ranch Hand accepted an invitation and participated in the 2002 follow-up examination. A matched cohort of Comparisons was chosen for this Ranch Hand. The Original Comparison refused, but a Replacement Comparison accepted an invitation and participated in the 2002 follow-up examination. This new Ranch Hand, his Original Comparison, and the participating Replacement Comparison are all included in the "New to Study" line for the 2002 follow-up examination in Tables 5-1, C-1, C-2, C-3, and C-4.

5. Two Ranch Hands were assigned to the 309th Air Commando Squadron but not assigned to the Special Aerial Spray Flight, thus they were misclassified as Ranch Hands in 1982. These Ranch Hands and their matched Comparisons (two Original Comparisons and one Replacement Comparison) were considered "ineligible" and excluded from further analysis. This change affects Tables 5-1, C-1, C-2, C-3, and C-4.

5.5.2 Analysis of Refusals

Of the 1,043 Ranch Hands and 2,044 Comparisons eligible for the 2002 follow-up examination, 262 Ranch Hands and 778 Comparisons (349 Original and 429 Replacement) refused. Their reasons for refusal are summarized in Table 5-3. The "no health match" potential Replacement Comparisons and those not located or contacted, as summarized in Table 5-1, are not shown in Table 5-3 and are not used in the analysis of refusals that follows. They may have been willing to participate, but were excluded by the specifications of the study protocol or the inability to contact them.

As shown in Table 5-3, a greater percentage of Comparisons than Ranch Hands refused (31.9% versus 25.1%), and a greater percentage of Replacement Comparisons than Original Comparisons refused (45.1% versus 31.9%). Of the total invited, nearly the same percentages of Ranch Hands, Original Comparisons, and Replacement Comparisons refused due to health reasons (5.4%, 5.1%, and 5.6%, respectively). More Replacement Comparisons than Ranch Hands or Original Comparisons declined due to "job commitments," "no time," or "travel distance or family concerns." In addition, more Replacement Comparisons (16.1%) than Original Comparisons (7.3%) were "passive refusals," indicating that this group of Comparisons did not respond to formal correspondence from the National Opinion Research Center (NORC) or the Air Force. More Original Comparisons were hostile refusals (9.5%) than either Replacement Comparisons (6.3%) or Ranch Hands (5.8%).

Table 5-3. Reasons for Refusal by Group

Reason	Ranch Hand n	Ranch Hand %[a]	Original Comparison n	Original Comparison %[a]	Replacement Comparison n	Replacement Comparison %[a]	Total n	Total %[a]
	Group							
Passive Refusal	64	6.1	80	7.3	153	16.1	297	9.6
Hostile	61	5.8	104	9.5	60	6.3	225	7.3
Health Reasons	56	5.4	56	5.1	53	5.6	165	5.3
No Interest or No Time	29	2.8	54	4.9	75	7.9	158	5.1
Job Commitment	15	1.4	24	2.2	42	4.4	81	2.6
Travel Distance, Family Concerns	12	1.2	14	1.3	24	2.5	50	1.6
Dissatisfaction with U.S. Air Force (USAF) or U.S. Government	7	0.7	6	0.5	5	0.5	18	0.6
Confidentiality, Adverse Impact on Career	6	0.6	2	0.2	3	0.3	11	0.4
Financial Hardship	4	0.4	2	0.2	4	0.4	10	0.3
Dissatisfaction with AFHS	3	0.3	1	0.1	5	0.5	9	0.3
Fear of Physical Exam	0	0.0	2	0.2	2	0.2	4	0.1
Dissatisfaction with Previous Exams	2	0.2	0	0.0	0	0.0	2	0.1
Other	3	0.3	4	0.4	3	0.3	10	0.3
Total	262	25.1	349	31.9	429	45.1	1,040	33.7
Total Eligible	1,043		1,093		951		3,087	

[a]Percent of veterans eligible to participate.

Table 5-4 summarizes reasons for refusal by group, age, military rank, and race. Reasons for refusal have been collapsed into the following five categories:

1. Health (health reasons)

2. Logistics (job commitment, no time or interest, travel distance or family concerns, confidentiality, or financial hardship)

3. Passive (passive refusal)

4. Hostile (hostile refusal)

5. Other (fear of physical examination; dissatisfaction with the USAF, U.S. Government, the AFHS, or previous examinations; confidentiality; or other reasons).

Table 5-4. Reasons for Refusal by Group, Age, Military Rank, and Race

| | Reason for Refusal | | | | | | | | | | | |
| | Health | | Logistics | | Passive | | Hostile | | Other | | | Unadjusted |
Category	n	%	n	%	n	%	n	%	n	%	Total	p-Value
Ranch Hand	56	21.4	60	22.9	64	24.4	61	23.3	21	8.0	262	<0.001**
Comparison	109	14.0	239	30.7	233	29.9	164	21.1	33	4.2	778	
Born Before 1942	136	25.6	138	25.9	119	22.4	111	20.9	28	5.3	532	<0.001**
Born in 1942 or After	29	5.7	161	31.7	178	35.0	114	22.4	26	5.1	508	
Officer	60	19.0	75	23.8	52	16.5	104	33.0	24	7.6	315	<0.001**
Enlisted	105	14.5	224	30.9	245	33.8	121	16.7	30	4.1	725	
Black	12	18.2	18	27.3	26	39.4	10	15.2	0	0.0	66	0.084
Non-Black	153	15.7	281	28.9	271	27.8	215	22.1	54	5.5	974	
Total	165	15.9	299	28.8	297	28.6	225	21.6	54	5.2	1,040	

Note: Percentages represent the percent of total refusals.

**: Statistically significant (p-value≤0.010).

Age, military rank, and race have been dichotomized for analysis purposes (born before 1942 and born in or after 1942; officer and enlisted; Black and non-Black, respectively). As noted in Table 5-3, of the total number of veterans invited, nearly the same percentages of Ranch Hands, Original Comparisons, and Replacement Comparisons refused due to health reasons (5.4%, 5.1%, and 5.6%, respectively). Based on only refusing veterans, and without adjustment for age, military rank, or race, the association between reason for refusal and group was significant (p<0.001). Excluding veterans who refused for other reasons described above, Ranch Hand refusals were almost evenly distributed among health reasons, logistical reasons, passive refusals, or hostile refusals. The Comparisons, however, tended to be passive refusals (29.9%) or refuse for logistical reasons (30.7%) more often than being hostile or refusing for health reasons. Therefore, hostile refusals and refusals for health reasons were a smaller percentage of the total number of Comparison refusals, which caused the significant difference in the distribution of refusals between groups. A test of association between reason for refusal and group (adjusted for age, military rank, and race) was performed and also found to be significant (p<0.001) due to the majority of Comparisons being either passive refusals or refusing for logistical reasons.

There was a significant association between reason for refusal and age (p<0.001) and between reason for refusal and military rank (p<0.001). Younger veterans (born in 1942 or after) were less likely to refuse for health reasons than older veterans (5.7% versus 25.6%). Younger veterans were more likely to be passive refusals (35.0% versus 22.4%) or refuse for logistics reasons (31.7% versus 25.9%). Officers were more likely to be hostile refusals than enlisted men (33.0% versus 16.7%) and were less likely to refuse because of logistics reasons (23.8% versus 30.9%) and to be passive refusals (16.5% versus 33.8%) than enlisted personnel. No significant association was found between reason for refusal and race (p=0.084).

5.5.2.1 Passive Refusals

A veteran was classified as a passive refusal if he was scheduled for a physical examination but twice cancelled the appointment or failed to appear for it. A veteran also was classified as a passive refusal for other reasons, including the inability to contact the participant directly because of the presence of a "gatekeeper" (see Section 5.4.1). A veteran was designated as a final passive refusal after a minimum of three contacts with a gatekeeper and failure to reach the participant by other means. Up to eight gatekeeper contacts were allowed if the scheduling supervisor decided additional attempts were still warranted. Passive refusals were provided with the toll-free number for the study and allowed to volunteer to participate at any time.

For the 2002 follow-up examination, the Air Force introduced a procedure to facilitate the scheduling process for those potential participants who refused to participate in the 1997 follow-up examinations. All refusals from the 1997 follow-up examination were sent a letter by the Air Force 6 to 9 months prior to the beginning of the scheduling process in March 2002. The letter asked each refusal in 1997 if he wished to participate in the 2002 follow-up examination. If the veteran did not wish to participate in the 2002 physical examination process, he was asked to return a card that was enclosed with the letter stating his wishes and to provide a reason for his nonparticipation. He was given the toll-free number and invited to contact the AFHS if he changed his mind. Veterans who did not return the card were classified as passive refusals.

Passive refusals accounted for 28.6 percent of the refusals at the 2002 follow-up examination. As described above, 29.9 percent of Comparisons were classified as passive refusal, whereas 24.4 percent of Ranch Hands were designated as passive refusals.

5.5.2.2 Hostile Refusals

Hostile refusals accounted for 23.3 percent of refusing Ranch Hands and 21.1 percent of refusing Comparisons for the 2002 physical examination. As shown in Table 5-5, 197 veterans (139 Comparisons and 58 Ranch Hands) were initially classified as hostile refusals during the 1992 physical examination process. Five additional veterans were added to the list of hostile individuals after the 1992 report was completed to bring the total to 202 individuals. Between the 1992 and 1997 examinations, this list of 202 veterans was reviewed and some individuals were redesignated as refusals that should be contacted for the 1997 follow-up examination. Some hostile individuals on this list also contacted the Air Force and expressed a desire to participate in the 1997 follow-up examination. Consequently, 17 veterans were removed from the list of hostile individuals. Six additional veterans on the list of hostile individuals died between the 1992 and 1997 follow-up examinations. The list of 202 hostile individuals was therefore reduced to 179 veterans that were not to be contacted by schedulers for the 1997 examination. During the course of the 1997 examination, 21 additional veterans were designated as "newly" hostile individuals, resulting in a total of 200 veterans designated as hostile for the 1997 follow-up examination, as shown in Table 5-5.

Of the 200 veterans who were designated as "hostile" for the 1997 physical examination, six veterans died between the 1997 and 2002 physical examination, one veteran who was previously designated as hostile asked to be and was allowed to become part of the 2002 follow-up physical examination, and one veteran who was previously designated as hostile was designated as ineligible (see Section 5.5.1). Consequently, 192 of the 200 previously designated hostile veterans were considered hostile as the 2002 physical examination process began. A total of 33 additional veterans were designated as hostile, based on contacts with these individuals by either mail or telephone, bringing the total of hostile veterans to 225 at the end of the 2002 follow-up physical examination process.

5.5.2.3   Reasons for Refusal Across AFHS Examinations

The reasons for refusal for the baseline, 1987, 1992, 1997, and 2002 examinations are shown in Table 5-5, presented separately for Ranch Hands and Comparisons. The reasons for refusal to participate in the 1985 examination are not addressed in Table 5-5 because the data were not collected in a manner consistent with that in the other examinations. In 1985, the data were collected verbatim as part of the record of telephone contacts. Therefore, no meaningful comparisons can be made between the 1985 study data on refusals and other years. Table 5-5 shows a consistent increase in total refusals across time. Of particular note is the steady increase in refusals for health reasons.

5.5.3   Replacement Comparisons

As stated previously, the process of choosing replacements for Original Comparisons who refused, matched on health status, as well as age, race, military rank, and occupation, was maintained at the 2002 follow-up examination. The reported health status of new replacements was obtained at the time of telephone scheduling. At the 2002 follow-up examination, 437 Replacement Comparisons were fully compliant (see Table 5-1). Table 5-6 summarizes the health-matching results for the 56 Replacement Comparisons invited to the study for the first time in 2002 (see Table 5-2) and their replaced Original Comparisons.

Of the 56 Replacement Comparisons, 35 were matched perfectly on health status to the Original Comparisons. Two additional Replacement Comparisons were matched according to the dichotomized health status indicated in the study protocol. Nineteen Original Comparisons (labeled "Unknown") did not provide a self-perception of health. The health status of the 19 Replacement Comparisons is shown in Table 5-6.

At the 2002 follow-up examination, 166 Original Comparisons were deceased, 7 could not be located, and 349 refused (see Table 5-7). The entire matched set of replacement candidates for each noncompliant Original Comparison was reviewed to determine if the appropriate replacement strategy was followed. Results are presented in Table 5-7. Of the 522 Original Comparisons who were not fully compliant for the 2002 follow-up examination, 316 compliant replacements were found. A total of 152 matched sets were closed because all previously invited Comparisons were deceased and, consistent with the protocol, no replacements were to be contacted, or because all replacements were contacted and no replacements were found that were willing to participate or were able to be health matched. No Replacement Comparisons were contacted for 13 of the noncompliant Original Comparisons. A review of the record of telephone calls showed that all 13 had declined late in the scheduling process. For 41 of the noncompliant Original Comparisons, some replacements, but not all, were contacted and none complied. A review of the cohort of the 41 Original Comparisons, where replacement contact was not fully exhausted, showed that the Original Comparison or one or more of the Replacement Comparisons also had declined late in the process. It is noted that all compliant Ranch Hands were included in the analysis, regardless of whether they had a matched Comparison.

Table 5-5. Reasons for Refusal by Group and Year

Reason	1982				1987				1992				1997				2002			
	Ranch Hand		Comparison		Ranch Hand		Comparison		Ranch Hand		Comparison		Ranch Hand		Comparison		Ranch Hand		Comparison	
	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]
Passive Refusal	9	0.7	15	0.9	40	3.4	78	4.5	41	3.6	96	5.5	23	2.1	42	2.2	64	6.1	233	11.4
Hostile	n/a	0.0	n/a	0.0	n/a	0.0	n/a	0.0	58	5.0	139	7.9	55	5.0	145	7.6	61	5.8	164	8.0
Health Reasons	10	0.8	7	0.4	11	0.9	16	0.9	19	1.7	21	1.2	42	3.8	66	3.4	56	5.4	109	5.3
No Interest or No Time	53	4.4	154	9.3	28	2.4	79	4.6	13	1.1	50	2.8	26	2.4	74	3.9	29	2.8	129	6.3
Job Commitment	29	2.4	80	4.8	32	2.7	61	3.5	31	2.7	53	3.0	33	3.0	104	5.4	15	1.4	66	3.2
Travel Distance, Family Concerns	4	0.3	21	1.3	5	0.4	17	1.0	8	0.7	17	1.0	14	1.3	42	2.2	12	1.2	38	1.9
Dissatisfaction with USAF or U.S. Government	5	0.4	0	0.0	10	0.8	11	0.6	6	0.5	10	0.6	1	0.1	6	0.3	7	0.7	11	0.5
Confidentiality, Adverse Career Impact	11	0.9	15	0.9	1	0.1	4	0.2	1	0.1	2	0.1	5	0.5	5	0.3	6	0.6	5	0.2
Financial Hardship	n/a	0.0	n/a	0.0	1	0.1	1	0.1	2	0.2	2	0.1	1	0.1	1	0.1	4	0.4	6	0.3
Dissatisfaction with AFHS	n/a	0.0	n/a	0.0	n/a	0.0	n/a	0.0	n/a	0.0	n/a	0.0	3	0.3	8	0.4	3	0.3	6	0.3
Fear of Physical Exam	6	0.5	6	0.4	1	0.0	4	0.2	0	0.0	3	0.2	1	0.1	2	0.1	0	0.0	4	0.2
Dissatisfaction with Previous Exams	n/a	0.0	n/a	0.0	0	0.0	1	0.1	3	0.3	5	0.3	5	0.5	6	0.3	2	0.2	0	0.0
Other	0	0.0	3	0.2	42	3.5	88	5.1	2	0.2	16	0.9	18	1.6	47	2.4	3	0.3	7	0.3
Total	127	10.5	301	18.2	171	14.4	360	20.8	184	16.0	414	23.5	227	20.6	548	28.6	262	25.1	778	38.1
Total Invited	1,207		1,657		1,188		1,730		1,149		1,761		1,101		1,919		1,043		2,044	

[a] Percent of veterans eligible to participate.
n/a: Not applicable or not available.

Table 5-6. Self-reported Health Status of Original Comparisons and Their Replacements

Replacement's Reported Health	Original Comparison's Reported Health					
	Excellent	Good	Fair	Poor	Unknown[a]	Total
Excellent	3	0	0	0	5	8
Good	1	23	0	0	8	32
Fair	0	0	7	1	4	12
Poor	0	0	0	2	2	4
Total	4	23	7	3	19	56

[a]Includes four hostile respondents, three deceased veterans (each of which had additional refusing Replacement Comparisons), two veterans who could not be located, five passive refusals, and five respondents who refused but did not provide a health status.

Table 5-7. Matched Set Compliance of Noncompliant Original Comparisons

Matched Set Compliance	Compliance of Original Comparison			
	Refusal	Unlocatable	Deceased	Total
At Least One Compliant Replacement	272	7	37	316
All Contacted Replacements Noncompliant and No Uncontacted Comparisons Remain in the Matched Set or All Previously Contacted Comparisons Are Deceased	29	0	123	152
All Contacted Replacements Noncompliant and Other Uncontacted Comparisons Remain in the Matched Set	35	0	6	41
No Replacement Comparisons Contacted	13	0	0	13
Total	349	7	166	522

5.6 MATCHING OF SELF-REPORTED HEALTH STATUS

5.6.1 Self-reported Health Status of Refusals

Ideally, compliance bias between the groups should be assessed by comparing the health of refusing veterans to fully compliant participants with adjustment for the matching variables. The only current data available on the refusing veterans are self-reported responses to the health status question asked during the scheduling procedure.

Of the 1,040 refusals, reported health status, as obtained by telephone at the time of scheduling, was available for a total of 512 Ranch Hands and Comparisons. Table 5-8 summarizes their responses. Data were obtained from 150 (57.3%) of 262 refusing Ranch Hands and 362 (46.5%) of 778 refusing Comparisons. Among the 512 refusals responding to the health status question, there was no significant association between group and reported health (p=0.072).

Table 5-8. Reported Health Status of Refusals

Reported Health Status	Ranch Hand n	Ranch Hand %	Comparison n	Comparison %	Total n	Total %	Unadjusted p-Value
	Group						
Excellent	14	9.3	57	15.7	71	13.9	0.072
Good	84	56.0	192	53.0	276	53.9	
Fair	28	18.7	77	21.3	105	20.5	
Poor	24	16.0	36	9.9	60	11.7	
Total	150		362		512		

Note: Does not include 14 Ranch Hands and 80 Comparisons from whom health status was not provided, 56 Ranch Hands and 152 Comparisons who were hostile, and 42 Ranch Hands and 184 Comparisons who were passive refusals.

A test of association between reported dichotomized health status and group, age, military rank, race, and compliance was performed. The results of this test are shown in Table 5-9. For analysis purposes, reported health status was classified into two categories: excellent or good, and fair or poor. The covariates age, military rank, race, and compliance were dichotomized (born before 1942 and born in 1942 or after, officer and enlisted, Black and non-Black, and fully compliant and refusal, respectively). No significant association was found between group ($p=0.278$) or race ($p=0.833$) and reported health status. Age ($p=0.017$), military rank ($p<0.001$), and compliance ($p<0.001$) were associated significantly with reported health. Enlisted men were more likely to report fair or poor health than were officers (24.4% versus 12.0%). As expected, refusals (32.2%) and older veterans (21.6%) were more likely to report fair or poor health than were fully compliant (16.5%) or younger veterans (17.7%).

The association between reported health status and group, adjusted for age, military rank, race, and compliance was significant ($p=0.048$). Ranch Hands were more likely to report their health as fair or poor (21.0%) than Comparisons (19.1%). The adjusted association between reported health status and compliance was statistically significant ($p<0.001$), as were the adjusted associations between health status and age ($p<0.001$) and military rank ($p<0.001$).

Table 5-10 shows the reported health status versus compliance separately by group. For both Ranch Hands and Comparisons, significantly more refusals reported fair or poor health ($p<0.001$ for both groups) than fully compliant participants. When adjusted for age, race, and military rank, the relation between health status and compliance did not change significantly with group ($p=0.980$). This result showed that the difference in health status between refusals and fully compliant participants was similar between Ranch Hands and Comparisons.

Table 5-9. Reported Health Status by Group, Age, Military Rank, Race, and Compliance

| | Reported Health Status | | | | | |
| | Excellent/Good | | Fair/Poor | | | Unadjusted |
Category	n	%	n	%	Total	p-Value
Ranch Hand	731	79.0	194	21.0	925	0.278[#]
Comparison	1,242	80.9	293	19.1	1,535	
Born Before 1942	1,046	78.4	288	21.6	1,334	0.017*
Born in 1942 or After	927	82.3	199	17.7	1,126	
Officer	799	88.0	109	12.0	908	<0.001**
Enlisted	1,174	75.6	378	24.4	1,552	
Black	126	79.2	33	20.8	159	0.833
Non-Black	1,847	80.3	454	19.7	2,301	
Fully Compliant	1,626	83.5	322	16.5	1,948	<0.001**
Refusal	347	67.8	165	32.2	512	
Total	1,973	80.2	487	19.8	2,460	

[#]P-value=0.048, after adjusting for age, military rank, race, and compliance.
  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Table 5-10. Reported Health Status by Group

| | | Reported Health Status | | | | | |
| | | Excellent/Good | | Fair/Poor | | | Unadjusted |
Group	Compliance Status	n	%	n	%	Total	p-Value
Ranch Hand	Fully Compliant	633	81.7	142	18.3	775	<0.001**
	Refusal	98	65.3	52	34.7	150	
Comparison	Fully Compliant	993	84.7	180	15.3	1,173	<0.001**
	Refusal	249	68.8	113	31.2	362	

**: Statistically significant (p-value≤0.010).

5.6.2   Self-reported Health Status of Fully Compliant Participants

Tables 5-11 through 5-13 summarize the reported health status, medication use, and work loss of the fully compliant participants at the 2002 follow-up examination. Table 5-11 summarizes the reported health status of participants fully compliant with the 2002 physical examination. Among fully compliant participants, no significant association was found between reported health at the time of scheduling and group (Ranch Hand, Comparison) (p=0.367).

Table 5-11. Reported Health Status of Fully Compliant Participants

| Reported Health Status | Group | | | | Total | | Unadjusted p-Value |
| | Ranch Hand | | Comparison | | | | |
	n[a]	%	n[a]	%	n[a]	%	
Excellent	227	29.3	359	30.6	586	30.1	0.367
Good	406	52.4	634	54.0	1,040	53.4	
Fair	118	15.2	147	12.5	265	13.6	
Poor	24	3.1	33	2.8	57	2.9	
Total	775		1,173		1,948		

[a]Does not include two Ranch Hands and one Comparison who did not answer or refused to answer the question on reported health status at the time of scheduling for the 2002 follow-up examination.

Table 5-12 presents the results of reported medication use by group. At the 2002 follow-up physical examination, a greater percentage of Ranch Hands reported using medication than Comparisons (74.3% versus 70.3%), but the difference was nonsignificant (p=0.064). Use of medication increased in both groups since 1997. Approximately 72 percent of all participants reported medication use at the 2002 follow-up physical examination, as compared to 57 percent of participants at the 1997 follow-up examination. The increase in medication use between the 1997 and 2002 follow-up examinations was consistent between groups, however, with approximately 4 percent more Ranch Hands reporting the use of medication than Comparisons at both examinations (58.9% and 55.0% for Ranch Hands and Comparisons, respectively, at the 1997 follow-up examination).

Table 5-12. Reported Medication Use of Fully Compliant Participants

| Medication Use | Group | | | | Total | | Unadjusted p-Value |
| | Ranch Hand | | Comparison | | | | |
	n	%	n	%	n	%	
Yes	577	74.3	824	70.3	1,401	71.9	0.064
No	200	25.7	348	29.7	548	28.1	
Total	777		1,172		1,949		

Note: Two Comparisons did not take the 2002 follow-up examination questionnaire.

Table 5-13 shows reported work loss from illness or injury in the 6 months prior to the 2002 follow-up physical examination for fully compliant Ranch Hands and Comparisons. The difference in work loss between the two groups was nonsignificant (p=0.754).

Table 5-13. Reported Work Loss of Fully Compliant Participants

Work Loss	Ranch Hand n	Ranch Hand %	Comparison n	Comparison %	Total n	Total %	Unadjusted p-Value
Yes	82	17.7	135	18.6	217	18.3	0.754
No	380	82.3	589	81.4	969	81.7	
Total	462		724		1,186		

Note: Analysis does not include the following:

   17 unemployed (6 Ranch Hands, 11 Comparisons)
   707 retired (289 Ranch Hands, 418 Comparisons)
   39 who did not answer the question (20 Ranch Hands, 19 Comparisons)
   2 participants (both were Comparisons) who did not take the 2002 follow-up examination questionnaire.

5.7   CONCLUSION

A greater percentage of Comparisons than Ranch Hands refused and a greater percentage of Replacement Comparisons than Original Comparisons refused. Of the total invited, nearly the same percentages of Ranch Hands, Original Comparisons, and Replacement Comparisons refused due to health reasons (5.4%, 5.1%, and 5.6%, respectively). More Replacement Comparisons than Ranch Hands or Original Comparisons declined due to "job commitments," "no time," or "travel distance or family concerns." In addition, more Replacement Comparisons were "passive refusals," indicating that this group of Comparisons did not respond to formal correspondence through NORC or the Air Force. More Original Comparisons were hostile refusals (9.5%) than either Replacement Comparisons or Ranch Hands. Ranch Hand refusals were similarly distributed among health reasons, logistical reasons, passive refusals, and hostile refusals. The Comparisons, however, tended to be passive refusals or refuse for logistical reasons more often than being hostile or refusing for health reasons. Younger veterans were less likely to refuse for health reasons than older veterans and were more likely to be passive refusals or refuse for logistics reasons. Officers were more likely to be hostile refusals than enlisted men and were less likely to refuse because of logistics reasons and were less likely to be passive refusals than enlisted personnel.

In replacing noncompliant Original Comparisons, either compliant replacements were found or no replacement was necessary (i.e., the Original Comparison was deceased and no Replacement Comparison had been contacted previously) for approximately 89 percent of the Original Comparisons. For the remaining 11 percent of the Original Comparisons, a review of the record of telephone calls showed that the Original Comparison or one or more of the Replacement Comparisons had declined late in the scheduling and examination process.

Self-reported health status differed with age, military rank, and compliance status among those reporting their health status at the time of scheduling for the 2002 follow-up examination. After adjustment for age, military rank, race, and compliance status, Ranch Hands were found to be more likely to report fair or poor health than Comparisons. In both groups, veterans who refused were more likely to report fair or poor health than those who were fully compliant. This pattern of Ranch Hands reporting poorer health has been observed since the baseline examination. Using work loss and medication use as more objective indicators of health than health perception, no difference was seen in reported work loss or in medication use between Ranch Hands and Comparisons. The increase in medication use between the 1997 and 2002

follow-up examinations was similar in both Ranch Hands and Comparisons and the difference was nonsignificant. A further analysis of self-perception of health, as reported by fully compliant participants at the 2002 follow-up examination, is given in Chapter 9, General Health Assessment.

In summary, of the total invited, nearly the same percentages of Ranch Hands, Original Comparisons, and Replacement Comparisons refused due to health reasons. Further analysis suggested that, when combining fully compliant and noncompliant veterans and adjusting for age, military rank, race, and compliance status, Ranch Hands reported poorer health than Comparisons.

REFERENCE

1. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1982. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Study protocol. NTIS: AD A 122 250. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

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6   QUALITY CONTROL

Quality control (QC) and quality assurance (QA) procedures were planned for and implemented throughout the 2002 Air Force Health Study (AFHS), from project initiation to final product delivery and acceptance by the Air Force. In-depth discussions of those procedures can be found in the *Quality Assurance Plan for the Air Force Health Study 2002 Follow-up Effort*, delivered to the Air Force as Contract Data Requirements List Item B014.

QC is defined as the procedures put in place to ensure the quality of the data collected. QA refers to the management of those procedures. This chapter provides an overview of the specific QC and QA measures developed and used by the project team, specifically in the areas of questionnaire and physical examination QC, laboratory QC measures, data management QC, statistical QC, and administrative QA. The Air Force, Science Applications International Corporation (SAIC), the National Opinion Research Center (NORC), and Scripps Clinic all participated in the formulation and implementation of the QC and QA procedures described in this chapter.

6.1   QUESTIONNAIRE QC

6.1.1   Design

For the baseline and subsequent follow-up examinations, the baseline and interval questionnaires were administered in person. In the examinations prior to 1997, the questionnaires were administered in hard copy and the data collected were keyed into the final SAS[1] data set. For the 1997 and 2002 follow-up examinations, the interview responses were obtained electronically on laptop computers using a computer-assisted personal interviewing (CAPI) data collection technique. As an alternative to paper questionnaires, CAPI allowed improved accessibility to data and made the interviewing process less burdensome to the interviewee.

Effective CAPI design was the first step in QC of the data collection. By combining the two steps of data collection and data entry, the CAPI technique eliminated one possible source of recording error—keying in the data. Further, the logic checks, range checks, and intervariable consistency checks programmed into the CAPI system placed constraints on what the interviewer could type or select for any particular question during the interview. These constraints limited keystroke errors and data problems arising from the interview itself. The structure of the CAPI system ensured that skip patterns were followed correctly and that no questions were left unanswered. In certain sections of the questionnaire, CAPI offered significant enhancements to the flow and accuracy of the questionnaire over a paper-and-pencil execution. These enhancements included automatic unit conversions and elimination of multiform cross-references. These benefits were most notable in the calculations of alcohol and tobacco use and in updating information for children born prior to the last interview.

Using a process of reviewing, commenting, and concurring, Air Force researchers and NORC designers incorporated new questions and streamlined existing questions when possible. The goal was to create a cohesive instrument with questions grouped logically by subject because a cohesive questionnaire would enhance the participant's focus on the subject being discussed and his understanding of the questions. By incorporating data already collected into the questionnaire, NORC was able to program CAPI to skip over questions to which the participant had provided an answer in an earlier follow-up examination. For example, participants previously reporting their mother as deceased were not asked if she was alive;

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[1] SAS and all other SAS Institute, Inc., product and service names are registered trademarks or trademarks of SAS Institute, Inc., in the USA and other countries.

however, participants previously reporting their mother as alive were asked. Similarly, if participants had previously provided the names of their siblings, these names were not re-asked, although the vital status of the siblings was updated. These and other streamlining improvements decreased the participants' frustrations with the examination process by eliminating question redundancy, providing a logical sequencing of questions, and decreasing the time spent by the participant.

An additional benefit of the CAPI questionnaire was the ability to print selected participant responses for use by the debriefing physicians. The layout and appearance of the printouts were improved for the 2002 follow-up examination, making them easier for the debriefing physicians to read.

6.1.2 Data Collection

NORC recruited and trained 10 interviewers and 1 field manager to administer the baseline and interval questionnaires. The interviewer training program comprised the following:

- A general interviewing training for new-to-NORC interviewers

- A home-study assignment prior to attending training

- A 3-day intensive training in March, which included daily homework assignments and a mandatory certification test afterward

- A 2-day refresher training in April followed by another mandatory certification test.

A minimum number of interviewers were selected to reduce variability between interviewing techniques. The interviewers were blind to the participants' exposure status, thus avoiding bias.

The field manager, who supervised the interviewing at the examination site, observed the work of all interviewers and presented formal evaluations of their performances to the Air Force each quarter. Interviewers were evaluated on their ability to control the interview and to probe incomplete answers in a neutral manner. They also were graded on their vocal quality, reading quality, and on their use of associated forms and documents. The interviewers were graded on a standardized scale of 1 to 4, where 1 indicated that the interviewer's performance needed improvement, 2 was acceptable, 3 was good practice, and 4 was exceptional performance with no errors. Interviewers typically received a grade of 3 or 4, but there were three cases in which a grade of 1 was assigned. In one instance, a new interviewer was added to the team and needed some additional practice to become more familiar with the questionnaire to improve her reading of the questions. In the other two instances, the new interviewer and an experienced interviewer who had returned from vacation were asked to focus on their completion of some of the associated forms and documents. Both of these interviewers successfully completed their retraining.

Interviewers were required to regularly report questions or problems experienced while executing the questionnaires. "CAPI Problem Forms" and "Policy Decision Forms" were distributed for interviewers to complete, and these forms were faxed daily to the data collection task leader at NORC headquarters in Chicago, Illinois. Items reported on the forms included the following: (1) mistakes made and not corrected during the interview, (2) conditions reported by the participant after the interview was over, (3) technical problems with the CAPI instrument, and (4) problems with the printout for the debriefing physician. The data collection task leader corrected problems when necessary and provided assistance to interviewers in handling confusing or unusual situations. Interviewers were sensitive to participants' reactions to the questionnaires. If interviewers felt that a participant failed to understand or respond to the questions acceptably, due to evasion, age, impaired memory, or disinterest, they recorded these observations in the interviewer comments for the associated question.

6.1.3 Processing and QA of Questionnaire Data

Completed questionnaire data were transmitted daily via modem from the La Jolla, California, site to the receiving computer system in Chicago. As interviews were completed on the laptop computers at the site office, the CAPI system selected the newly completed cases, encrypted the interview data, and transmitted the interview data to the NORC modem pool in Chicago. Once in Chicago, the interview data were unencrypted, archived on a devoted volume of the NORC UNIX computer, and copied to the NORC wide area network. Each CAPI interview comprised one multiple-record ASCII file representing the participant's answers to questions. Using a standard code, the ASCII files were converted to SAS® data sets. Programmers then read the horizontal files into SAS® and printed frequencies of all variables. Case data received in Chicago were reconciled regularly with the completion log at the interviewing site.

Some of the QC steps used in converting CAPI files to the SAS® data files include the following:

1. The case IDs of all completed interviews in the SAS® file were compared to the log of completed interviews kept at the site office. This ensured that all completed cases were received and that there were no duplicates.

2. The SAS® variables were compared to a hard-copy representation of the CAPI to ensure that all questions in the interview were present in the SAS® data file.

3. The response frequencies were reviewed to ensure that the questionnaire was operating correctly, no data items were skipped, and no data items were truncated.

One of the goals in the conversion process was to replicate, to the maximum extent possible, the variable names, formats, and structures used for the 1997 follow-up examination. To accommodate this goal, additional "post-processing" programs were created. The post-processing included renaming variables, assigning the appropriate variable labels and value labels, creating variables based on values of answers to more than one question (such as calculations of cigarette use), and merging variables collected outside the interview into the data set.

Several steps were taken to ensure that the SAS® data file created from the post-processing programs contained the correct information:

- A list was created that mapped CAPI variables to SAS® variables. This allowed the NORC staff to ensure that variables were named properly and that all required variables were included in the SAS® data set.

- The list of SAS variables from the 2002 data set was compared to that from the 1997 data set to ensure the inclusion and correctness of all necessary variables.

- Format statements and frequencies were proofed against three representations of the questionnaire (the CAPI form, the 1997 hard copy representation, and the 1992 hard copy) to detect problems.

- Cross-tabulations and printouts of data items at the case level were generated to investigate complicated questions, such as whether a calculation was working correctly or why there was a missing value in a certain variable.

- Continuous reviews of the frequencies were performed until no more errors were detected.

- A cumulative data set of all interviews completed to date, accompanied by a footnote file explaining any anomalies or programming issues still to be resolved, was delivered quarterly and then monthly to the Air Force for review. All errors identified by the Air Force were

corrected by NORC, the data set was corrected and delivered a final time, and the corrections were accepted.

Response frequencies for all data fields were reviewed regularly to ensure that data for all variables were captured, answers made logical sense, and the skips and checks programmed by CAPI were operating correctly. These QC checks revealed a problem in the programming of two new preload variables that determine entry into two series of questions: the "Combat Questionnaire" and the "Ever Drink Herbicide" question. Some participants who should have been asked these questions skipped them, and some participants who did not need these questions were asked them. The following three steps taken to correct this situation are more fully documented in NORC's Methodology Report:

1. Immediately upon discovery of the problems, a hard-copy version of these questions was distributed to NORC's interviewers so that in the upcoming groups information would be obtained from the required participants in the event that the CAPI system did not properly direct them to the questions.

2. The questionnaire code was reviewed and corrected, and the revised CAPI instrument was transmitted to the laptops.

3. NORC schedulers telephoned the 15 participants who should have been asked these questions but were not in order to collect the information. Data were successfully retrieved from all but one of these participants. These data were then merged into the full questionnaire database.

To increase the quality of the spelling on verbatim data, NORC implemented a spellchecking process for the 2002 follow-up examination. Interviewers were encouraged to take the time to spell carefully and to consult a spelling list of common medical terms to the extent that this did not interfere with the interview or increase the participant's burden. The spellchecking of the collected data occurred during the data review process. Data supplied for verbatim variables were extracted from the SAS® data and loaded into a Microsoft® Excel spreadsheet. A data clerk ran the Microsoft® Excel spellchecker program using a dictionary customized to include common medical terms and medications. The clerk could agree with Microsoft's suggested change, make his or her own change, or leave the supplied data unchanged. Both the original collected data and the spellchecked version of the data were delivered in the final data set.

During final QA of the questionnaire data, it was discovered that a series of three questions meant to assess self-reported intermittent claudication and vascular insufficiency were not administered as planned. The question "Do you get a pain in either or both of your legs while walking?" was asked of all participants. A total of 415 participants responded affirmatively. For these 415 participants, the second question, "Does this pain ever begin when you are standing or still sitting?", was subsequently asked. A total of 254 participants replied "yes" to this question and 161 participants replied "no." The participants who responded "no" to this question were supposed to be asked the third question, "Do you get this pain in either or both of your calf muscles?" Because of an unintentional change to the programming code, however, this question was asked of the participants who replied "yes" to the second question and not of the participants who responded "no." The participants who responded "no" to the third question were telephoned by Air Force staff and their responses to the third question of the series were collected.

6.2 PHYSICAL EXAMINATION QC

The Scripps Clinic selection process for all personnel who were to interact directly with the participants ensured a high-quality physical examination. Each staff member was hand-selected for the AFHS on the basis of expertise, experience, and a commitment to remain with the study throughout the examination process. Further, the Air Force reviewed the credentials of all key staff members and approved their participation in the study.

A complete examination test was held. Eleven volunteers completed the physical examinations, interviews, psychological tests, and laboratory analyses several weeks before the scheduled start of the examination. A twelfth volunteer completed the psychological tests only. All aspects of patient contact were reviewed: the initial inbriefing of the participants, the logistics of transportation and patient flow within the clinic, and the final outbriefing by the internist.

During the actual examinations, refinements were made whenever operational problems were detected. Whether detected by the Scripps Clinic staff, the Air Force onsite monitor, or the participants, problems were addressed during periodic clinical QA meetings of key Scripps staff.

During the physical examination, the identification of one chest x-ray film was found to be questionable because of improper labeling. The overall chest x-ray assessment was used in the analysis of the pulmonary function, and the participant whose x-ray film was in question was contacted and the x ray was reaccomplished.

Following examination of each participant group, the Scripps Clinic staff reviewed all physical examination forms for omissions, incomplete examinations, and inconsistencies. When issues were found, the examiners or technicians were contacted to correct the data. Special effort was made to complete this review while the participants were at the examination site. In all cases in which data were corrected, the form was initialed by the doctor or technician making the correction. (This subject is discussed in more detail in Section 6.4 of this chapter.) An optical scanner read all mark-sense physical examination forms as an ongoing QA of form completion.

The Air Force onsite monitors and the Scripps Clinic administrative team monitored compliance with the physical examination process. The Scripps Clinic Chief of Medicine and the SAIC Project Manager conducted additional periodic inspections. All such clinical reviews were performed unobtrusively and with the full consent of the participant; suggestions or corrections to the examination procedure always were discussed privately with the attending physician. These inspections emphasized aspects of clinical techniques, sequence, and completeness of the clinical data with respect to the examination forms and the blindness of the examinations. Of particular note were the detailed daily log entries of the Air Force monitors. These entries ensured continuity of knowledge (the monitors rotated approximately every 2 weeks) by documenting daily activities and, when needed, recording events requiring follow-up by either the Air Force or SAIC.

Establishing a rapport with each study participant was a primary goal of all the organizations involved in the study. Although this may not be a traditional QA parameter in most research studies, it is paramount in the AFHS. Maintaining participant satisfaction encourages the participants to continue in the study, thus avoiding the need for substantial replacement, which can reduce future statistical power or introduce bias, or both. Therefore, every staff member emphasized courtesy, empathy, and personalized treatment of each participant.

Participants were asked to fill out an evaluation form after completing their 2002 follow-up physical examinations. The participant evaluations provided insight into the participants' experiences, including strong points of the programs and areas in need of improvement. These forms were reviewed by all study management staff.

Based on the participants' evaluation forms, 80.9 percent evaluated their overall clinic experience as excellent, and 17.8 percent classified it as good. No participants felt that the overall clinic experience was unsatisfactory, and 1.3 percent of the participants rated it as satisfactory. These evaluations are charted in Figure 6-1.

Figure 6-1. Participant Evaluations of the 2002 AFHS Clinic Experience

6.3 LABORATORY QC

Before the examination began, specific QC laboratory procedures were designed, developed, and implemented to detect problems related to test and assay performance, validity of reagents, analysis of data, and reporting of results. All laboratory assays for the examination were performed with state-of-the-art laboratory equipment and techniques. Laboratory facilities all had the equivalent of National Institutes of Health Biosafety Level 2 approval ratings and were certified by the College of American Pathology.

6.3.1 QC Procedures for the Clinical Laboratory

The following list outlines the tests performed and the methods and equipment used:

- Hematology assays were performed on Abbott Cell-Dyn 4000 equipment.

- Erythrocyte sedimentation rate (ESR) determinations were performed using the Ves-Matic™ equipment.

- Coagulation assays were performed using Dade Behring Blood Coagulation System equipment.

- Biochemical assays were performed using the Dade Behring Dimension® RxL automated chemical analyzer.

- Insulin and C-Peptide assays were performed on the DPC Immulite chemistry analyzer.

- Hemoglobin A1c was performed on Bio-Rad Variant equipment.

- Radioimmunoassays and immunofluorescent assays were performed with standard test kits.

- Immunochemistries were performed using the Bayer ADVIA Centaur® instrument.

- Occult blood tests were performed manually.

- Hepatitis A assays were performed using Abbott Commander® equipment.

- Monospecific antibodies were used for immunoglobulin assays using the Beckman Coulter IMMAGE® system.

- T & B lymphocytes were analyzed on Becton Dickinson FACScan equipment.

- Blood cell counts were performed with standard microscopy.

- All urinalyses were performed using Bayer Atlas® equipment.

- All other assays were performed using industry-standard equipment and techniques.

All laboratory operations were controlled with the use of an integrated medical laboratory management information system that incorporated direct device-to-database interfaces for automated testing equipment. Laboratory technologists performed data entry for manual tests. An automated audit trail and a set of comments for technologist remarks were kept for each test so that any QC results could be retraced.

Procedural QC included using the same instrument and reagents from the same lot numbers whenever possible throughout the examination. If single lots were unavailable, analyses were conducted to calibrate subsequent lots and establish target levels and associated standard deviations. Strict standards of calibration for all automated laboratory equipment were maintained at all times.

Tri-level or bi-level controls were used as the primary means for monitoring the quality of all tests. On every group of participant samples, one control (low, medium, or high) was run at the start, after every ninth sample, and at the end of each test run. Each tri-level control was used before repeating it in the run when more than 18 experimental samples were analyzed. In addition, split aliquots were created from every 10th participant sample and were analyzed separately to measure test reproducibility. In radioimmunoassays, all three control levels were run initially to validate the standard curve generated.

Scripps Clinic Medical Laboratory has defined quality requirements of accuracy above 99 percent and levels of precision above 97 percent. A variation of the Westgard Rules (1, 2) QC technique is routinely used in the Scripps Laboratory and was used for AFHS assays. In this variation, the 1_{2s} single rule and 4_{1s} multiple rule are used. The 1_{2s} rule indicates rejection of any run when the control value of any one of the three controls (low, mid, high) exceeds two standard deviations from the mean. The 4_{1s} rule indicates rejection of a run when four consecutive control measurements exceed one standard deviation on the same side. This approach ensures an effective system for reducing the probability of false rejection to the lowest acceptable level while maintaining error detection at more than 98 percent.

All QC data were analyzed and summarized in formal QC reports generated monthly. QC data were subjected to independent statistical analysis by the Air Force to produce and analyze time-dependent trends. For all equipment malfunctions or other exceptions, a formal QC exception report was prepared by the responsible individual and forwarded to the project management team. A summary of the coefficients of variation for each quantitative laboratory assay is presented in Appendix D. These coefficients of variation are given separately for each control level and lot.

During the period 21 August 2002 to 18 September 2002 the Ves-Matic™ 20 instrument that performs ESR on whole blood was inoperable. The Ves-Matic™ 20 ESR measures the ESR directly from the collection tube. Results equivalent to a 60 minutes ESR are available in 20 minutes. The back-up manual technique called the Modified Wintergreen method was employed during that period. There was a change in the quality control target and standard deviation during those dates.

6.4   MEDICAL DATA QC

6.4.1   Overview of QC Procedures

The QC procedures for the medical data included multiple checks at all stages of the examination, data collection, and data processing cycle. Figure 6-2 charts the QC process. Although improvements were made throughout the physical examination period, QC procedures for data collection, conversion, and integration were developed before the clinical examinations began. All data collection instruments were tested at the examination test conducted several weeks before the start of participant physical examinations. In addition, during the first 2 months of the clinical examinations, all data collection activities were routinely scrutinized to detect and correct procedural deficiencies. Other QC activities included the following:

- Automated QC techniques applied to laboratory data

- Clinical evaluations of all laboratory outliers

- Review of all physical examination findings by one of three internists

- Automated and manual data quality checking of hard copy against transcribed computer files.

Four interwoven layers of QC were instituted to ensure data integrity. These efforts focused on (1) data processing system design, (2) design and administration of all exams, (3) data completeness checks, and (4) data validation. In addition, Air Force project personnel reviewed all physical examination forms and entries. Forms that were found to be questionable, inaccurate, or incorrect were returned to Scripps Clinic for adjudication.

6.4.2   Data Processing System Design

Standards were established for data element formats (character or numeric), data element naming conventions, data element text labels, numeric codes for qualitative responses and results, QC range checks for continuous data elements, and QC validity checks for categorical data. A data dictionary provided detailed information on each data element.

A systems integration approach was applied to the design and implementation of data collection procedures so that data emanating from the physical examination, questionnaire, and laboratory were consistent in file format and structure. This approach was necessary to ensure that all data could be integrated into a single database for analysis.

Data collection forms were carefully designed to ensure that all required data elements would be collected in accordance with the study protocol and in a standardized format. These instruments were designed to reflect the order in which the examination itself would be administered and to provide for the sequential coding of information.

Figure 6-2. Physical Examination Form QC Process

Completed clinical examination forms were converted from hard copy to machine-readable images using optical mark reading (OMR) equipment. Verification procedures were performed to ensure that a uniquely identified participant record existed within each data file and that the appropriate number of responses for each applicable field was provided. Data files were then translated into a SAS® data set, verified against original data sheets, and corrected as necessary. All corrections to the original data sets were saved in the processing program, which was delivered to the Air Force for verification.

Next, the SAS® data sets were subjected to validity checks. All potentially conflicting results, as well as any data values falling at the extremes of expected ranges, were reviewed manually. Extreme values were verified against the original data forms and either corrected or documented as valid results. Potentially

conflicting results, either within one form or among forms, were returned to the examiners for review. These results were then documented as having been correctly recorded, corrected, or flagged for exclusion from analysis because of unresolvable examiner errors or omissions. This process was continued until all results were properly documented.

The validity checks were tested with the delivery of the first cumulative medical results data. At that time, it was discovered that some data were not properly cross-checked between collection forms. The discrepancies were adjudicated by the appropriate Scripps Clinic staff and corrected on the forms and in the database in accordance with the QC procedure. Additional QC steps were added to the procedures because of these discrepancies.

Once the edits were completed and the data verified, the "cleaned" files were transferred to the data analysis center for final inspection and integration into the study database. In this QC measure, descriptive analyses were run. The validation, correction, transmission, and analysis QC procedures were repeated as necessary to ensure that all extreme or suspicious values had been validated. As an additional measure of QC, cumulative result data sets were delivered quarterly during the physical examination phase for Air Force review. The data sets were finalized following the close of the physical examinations and before the start of statistical analysis. Figure 6-3 displays the process for cleaning and converting the collected data into final data sets.

6.4.3   Design and Administration of Physical and Psychological Examination Forms

The examination forms were designed to elicit all required data while minimizing recording time, enhancing comprehension, and automating data input. Customized mark-sense forms were developed and OMR technology was used to eliminate the risk of transcription errors. The use of mark-sense forms allowed computerized data files to be created directly from the raw data recorded on these forms.

As an added QA and QC measure, formal meetings were held with the examining physicians and technicians to review the data collection forms. These meetings were held by medical specialty so that the attending staff could review and make comments on their specific forms, as well as reach a consensus on diagnostic techniques and abbreviations.

QC procedures for all data collection instruments began with both manual and electronic reviews of each form as it was completed. A mark-sense reader was used at Scripps Clinic to scan for completeness and to conduct some broad-based logic checks. Special efforts were made to have any forms containing missing, incomplete, or contradictory examination results returned to the examining physician for completion before the participants left the site. Any questionable results or "hard-to-diagnose" conditions (such as heart sounds or peripheral pulses) were verified by the internist at the outbriefing. In addition, any differences in interpretation among examiners were identified, and adjustments in recording protocols and programmed data extraction were made as necessary. All examination forms were signed by the examining physician, and the examiner identification number was coded in the database.

6.4.4   Data Completeness Checks

Customized programming of the OMR allowed for the identification of those forms (and their corresponding data records) with missing responses, as well as those with multiple responses to questions that required a single response. The OMR scanner was programmed to reject forms that failed completeness and multiple response checks and to generate a control code for each rejected form. The control code identified the location of all verification checks failed for a given form.

Figure 6-3. Conversion and Cleaning Process for Medical Data

When a data collection form was rejected, the reason for the rejection was determined. The exact data element was then corrected by comparing the rejected form to the values recorded in the data record created by the scanner. Some of the rejected forms did not contain actual data errors, but rather anomalies created in using mark-sense forms for data collection. For example, the scanner incorrectly counted incompletely erased responses and missed responses marked with too little graphite. Failure of the form to provide the correct number of expected responses always resulted in rejection. These errors were resolved, as were the anticipated, more traditional errors.

Out-of-range results and data omissions were monitored to detect trends, possible bias situations, and other data-quality problems. This information was reviewed and relayed to examiners and internal auditors to assist in preventing or correcting chronic, but avoidable, problems. Refresher training was provided to examining physicians to avoid data omissions. Physicians were consulted to correct clinical data, and laboratory out-of-range results were reviewed for logical validity by an independent clinician.

6.4.5   Data Validation

Data files were examined in a series of verification and validation procedures developed to check the results within each participant's record for logical consistency and abnormal findings. Any records noted to have ambiguous findings, incongruent observations, extreme results, errors, or omissions were listed and submitted for review to a physician.

Certain data items were assigned codes to indicate that data values were not available. Some reasons for unavailable data included the following:

- Participant refusal

- Test not ordered (e.g., immunology tests, which were only ordered for a subset of the participants)

- Exemption from testing (e.g., exemption from postprandial glucose testing because of diabetes).

These unavailable data were excluded from subsequent analysis. The number of values not available for analysis is presented in each clinical chapter by variable.

As the examination portion of this study ended, an independent clinician analyzed laboratory outliers for logical validity. Each outlier was adjudicated using the following four codes:

1. Clinically explained or plausible (participant has single outlier)

2. Clinically explained or plausible (participant has multiple outliers)

3. Abnormal outlier not clinically explained but plausible

4. Abnormal outlier not clinically explained and not plausible.

In the 2002 follow-up examination, all potential out-of-range results were found to be clinically explainable or clinically possible. Therefore, no clinical laboratory data were excluded from the report analyses. Subjects with missing values were excluded if the value was required for the statistical model.

6.5   MEDICAL RECORDS CODING QC

SAIC forwarded completed physical examination records and questionnaire data to the Air Force at Brooks City-Base, Texas, for diagnostic coding and verification of all subjectively reported conditions. The Air Force used the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) for morbidity coding; the Systematized Nomenclature of Medicine for anatomic site coding; and the American Hospital Formulary Service for medication coding. Two medical records technicians independently processed each questionnaire and physical examination. Both codings were then subjected to a 100-percent QA review, during which every posted code was checked against medical records. A third medical records technician adjudicated any discrepancies.

6.6   STATISTICAL ANALYSIS QC

Specific QC measures were developed for the statistical analysis efforts. The tasks requiring QC included construction of databases for the analysis of each clinical chapter, the statistical analysis itself, and preparation of the clinical chapters.

Each specialized statistical database was constructed by defining and locating every variable within the many subparts of the composite database. Although the data had been subjected to QA procedures during collection, statistical checks for outliers and other improbable values were conducted. Anomalies

identified by the statisticians were discussed with those responsible for the data collection (i.e., NORC, Scripps Clinic, or the Air Force).

QA largely depended on regular communication and general agreement among statisticians. Several meetings and consultations between the Air Force team and SAIC statisticians were held in conjunction with the development of the data analysis plan. In addition, many telephone conversations took place during the course of the statistical analysis. Any problems identified in the statistical analysis were resolved through team discussion. Specialized SAS$^®$ programs were developed by the task manager for each type of analysis (exposure or dependent variable-covariate associations) and form of the dependent variable (continuous, dichotomous, polytomous). These programs allowed many of the results to be saved in a Microsoft$^®$ Excel spreadsheet, which was used to import the results into the final report, a Microsoft$^®$ Word document. The software was checked by comparing results from analyses on the same variable by different programs. These programs were adapted for use in all clinical areas by changing the data source, dependent variable, covariates, and exclusions so that a consistent statistical methodology could be applied to all clinical areas. Modifications to the programs were made only as necessary (e.g., a sparse number of abnormalities that necessitated the exclusion of a particular covariate). Each analysis and the summary statistics reported for the analysis were replicated independently by a statistician not directly involved in the analysis for the report. The analyses were conducted in accordance with the data analysis plan, which was reviewed extensively by SAIC and the Air Force. Throughout the 2002 follow-up examination effort, the Air Force and SAIC maintained duplicate databases. Upon completion of the analyses, SAIC delivered all analysis software and SAS$^®$ data sets for each clinical area to the Air Force for final review and archiving.

All tables and statistical results were checked against the computer output from which they were derived, and all statistical statements in the texts were checked for consistency with the results given in the tables. In addition, drafts of each chapter in this report were reviewed by the Air Force and SAIC investigators.

6.7   ADMINISTRATIVE QA

In recognition of the magnitude, complexity, and importance of the AFHS, SAIC created an internal Quality Review Committee (QRC). The QRC was established at the initiation of the 1985 follow-up examination and continued through the 1987, 1992, 1997, and 2002 follow-up examination. Its purpose was to provide general oversight to the AFHS program and advice on the appropriateness of program management and QC actions. The QRC comprised SAIC senior corporate personnel and consultants. These independent reviewers remained separate from the project management staff. The QRC met periodically to review study progress and any issues that either had an impact on study quality or were perceived as a potential problem. Members of the QRC also conducted first-hand evaluations of ongoing program operations.

REFERENCES

1. Westgard, J.O., and P.L. Barry. 1986. Cost-effective quality control: managing the quality and productivity of analytical processes. AACC Press: Washington, DC.

2. Westgard, J.O., J.J. Seehafer, and P.L. Barry. 1994. Allowable imprecision for laboratory tests based on clinical and analytical test outcome criteria. *Clinical Chemistry* 40:1909-14.

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7   STATISTICAL METHODS

7.1   INTRODUCTION

This chapter summarizes the statistical methods used in the analysis of Air Force Health Study (AFHS) 2002 follow-up examination data to investigate relations between the health status of the participants attending this examination and their corresponding group (Ranch Hand or Comparison) or serum dioxin estimates and measurements. Group contrast models were similar to analyses performed for the 1982 baseline and 1985, 1987, 1992, and 1997 follow-up examinations (1, 2, 3, 4, 5). Models relating health to dioxin estimates and measurements were based on analyses performed for the serum dioxin analysis report for the 1987 follow-up examination and the 1992 and 1997 follow-up examinations (4, 5, 6).

The statistical methods used in the analysis of AFHS 2002 follow-up examination data encompass four different forms of hypotheses or models applied to study endpoints. Each of these models specifies the study cohort or subset of participants included in the respective analyses together with the dioxin exposure or proxy estimates to be used in the analysis. The first model (Model 1) specifies contrasts between Ranch Hands and Comparisons using group as a proxy for exposure; it does not incorporate serum dioxin measurements. The remaining three models (Models 2, 3, and 4) all incorporate serum dioxin measurements. The four statistical models used in this report and described in this chapter are a legacy from previous reports. Other approaches have been used in articles by AFHS staff published in peer-reviewed scientific journals. Those approaches sometimes used different statistical models and different methods of adjustment, and were restricted by clinical area to fewer outcome variables. The statistical models summarized here are intentionally consistent with those used in previous reports, to enable comparisons of study results across time, but do not include adjustments for recently discovered confounding variables. A summary description of each of the four statistical models is provided in Section 7.2.

Each statistical model and exposure estimate combination was implemented for study variables and type of analysis (unadjusted or adjusted). The specific statistical procedures (e.g., analysis of variance or logistic regression) that were used are presented in Section 7.3. The relation between the factors that influence the use of a particular statistical procedure and the statistical procedure used is presented in Section 7.4, followed by a discussion of interpretive considerations in Section 7.5. Section 7.6 describes the contents of the tables used to report statistical analysis results throughout the report.

7.2   STATISTICAL MODELS AND ASSUMPTIONS

The statistical analyses in this report are based primarily on four statistical models, each using a different measure of exposure. The first model uses group and military occupation (officer, enlisted flyer, and enlisted groundcrew) to assess health effects and dose-response relations related to exposure. Serum dioxin measurements were not used in this model. The other three statistical models accounted for dioxin effects either through estimated initial dioxin levels for Ranch Hands or using 1987 serum dioxin levels for Ranch Hands and Comparisons to assess health effects and dose-response relations related to exposure. Analyses based on these statistical models were carried out both unadjusted and adjusted for covariates.

7.2.1 Model 1: Group and Military Occupation as Estimates of Exposure

This section describes the statistical model that used the exposure group (Ranch Hand, Comparison) to assess the relation between health status and dioxin exposure. Statistical analyses based on this model were termed "Model 1" in the assessment of the clinical areas. Analyses of this type are straightforward, easy to interpret, and well established in epidemiologic studies when a better measure of exposure is not available. In this statistical model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. As an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (officers, enlisted flyers, and enlisted groundcrew). As described in the serum dioxin analysis report for the 1987 follow-up examination (6), among Ranch Hands the average levels of exposure to dioxin were highest for enlisted groundcrew, followed by enlisted flyers, then officers.

Table 7-1 provides a description of Model 1 and gives the assumptions, advantages, and disadvantages for a continuously distributed health endpoint, y. The statistical model presented in Table 7-1 is unadjusted for any covariates—adjusted models are a straightforward extension. It should be noted that this statistical model is considered the "full model" in statistical terms and the coefficients corresponding to group, military occupation, and the interaction between group and military occupation are not estimable. Reparameterization must be performed to estimate a linear combination of these coefficients.

Table 7-1. Model 1: Assessing Health Versus Group Status in Ranch Hands and Comparisons: Assumptions, Advantages, and Disadvantages

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Model 1: $y = \mu + G_i + e$ **(All Ranch Hands and Comparisons)**

$y = \mu + G_i + O_j + (GO)_{ij} + e$ **(Ranch Hands and Comparisons by military occupation)**

where

y	=	health variable in group i and military occupation j
μ	=	intercept of the y-axis in the statistical model
G_i	=	effect due to group status (i = 1,2 – Comparisons, Ranch Hands)
O_j	=	effect due to military occupation (j = 1,2,3 – Officers, Enlisted Flyers, Enlisted Groundcrew)
$(GO)_{ij}$	=	interaction between group status and military occupation (i = 1,2; j = 1,2,3); used to examine Ranch Hand and Comparison differences for each military occupation
e	=	zero mean error.

Assumptions: Comparisons were unexposed and Ranch Hands were exposed.

For the purposes of investigating dose-response effects, enlisted groundcrew were more heavily exposed than enlisted flyers, and enlisted flyers were more heavily exposed than officers.

The error variance does not change with group status or military occupation.

Advantages: Easily interpretable.

Disadvantages: Results are biased toward the null hypothesis of no dioxin effect if unexposed Ranch Hands are misclassified (i.e., remain in the analysis as exposed Ranch Hands). It is not possible to fully distinguish unexposed Ranch Hands from exposed Ranch Hands.

An advantage of Model 1 is that it follows the original design of the study, contrasting Ranch Hand with Comparisons overall and by military occupation. A disadvantage of Model 1 is that no account is taken of the dioxin body burden of each individual. Approximately 40 percent of the Ranch Hand cohort has dioxin values less than 10 parts per trillion (ppt) (the 98th percentile of the dioxin distribution of Comparisons). Thus the potential bias toward the null due to misclassification on exposure may be severe. This potential bias is partially balanced by the group contrast within the enlisted groundcrew stratum because enlisted groundcrew Ranch Hand veterans have the highest median dioxin of the three military occupations. Misclassification is even possible within this stratum, however, because some Ranch Hand enlisted ground veterans have dioxin values less than 10 ppt.

7.2.2 Models 2 through 4: Serum Dioxin as an Estimate of Exposure

1987 dioxin levels were determined by the Centers for Disease Control and Prevention from serum samples taken from approximately 2,000 Ranch Hands and Comparisons at the 1987 follow-up examination. Additional serum samples were taken from selected Ranch Hands and Comparisons at the 1992, 1997, and 2002 follow-up examinations to provide insight on dioxin levels and the elimination of dioxin from the body, and to provide measurements for new subjects and those who were not previously measured.

Investigation of the mechanics of dioxin elimination is currently under study by the Air Force. Based on samples collected in 1982, 1987, 1992, 1997, and 2002, issues such as half-life estimation and first-order pharmacokinetic assumptions are being investigated.

7.2.2.1 Prior Knowledge Regarding Dioxin Elimination

Pharmacokinetic studies of dioxin elimination have been conducted based on repeated dioxin measurements in a subset of 343 Ranch Hand veterans. The term "elimination" denotes the overall removal of dioxin from the body. Section 7.2.2.1 presents analytic strategies based on assumptions and statistical models conceived after the first Ranch Hand pharmacokinetic study performed in 1996 and subsequently updated in 1999 (7). Available data have suggested that the dioxin elimination process is approximately first-order, based on measurements subsequent to the ingestion of dioxin by an individual (8). Data on 213 Ranch Hand veterans with dioxin measured in blood collected in 1982, 1987, 1992, and 1997 produced a half-life estimate of 7.6 years (7); this estimate was used in all calculations involving half-life. Pharmacokinetic studies (7) were restricted to 343 Ranch Hand veterans with 1987 dioxin greater than 10 ppt because it was thought this value represented an upper threshold for background exposure (as evidenced by the fact that 10 ppt was the 98th percentile of the Comparison dioxin distribution) and that the first-order elimination model did not hold at background levels. Subsequent analyses of dioxin elimination in Comparisons, however, have challenged this assumption (9). Nevertheless, 10 ppt has been interpreted as a threshold below which the first-order model does not hold. A Ranch Hand with dioxin less than 10 ppt may have been exposed to dioxin in Vietnam and his body burden decreased to a value less than 10 ppt since his service in Vietnam, or he may not have experienced increased dioxin exposure in Vietnam. Current data is not sufficient to resolve these two possibilities. Hence, the "Background" dioxin exposure category in Model 3 is probably comprised of a mix of individuals, some who experienced dioxin exposure in Vietnam and currently have a value less than 10 ppt and some who did not receive any appreciable dioxin exposure in Vietnam.

Analyses in this report based on Models 2 and 3 have assumed that the amount of dioxin in the body (C) decreases exponentially with time according to the statistical model $C = I \cdot \exp(-rt)$, where I is the initial level, $r = \log(2)/h$ is the elimination rate, h is the half-life, and t is the number of years from the end of the veteran's last qualifying tour of duty in Southeast Asia (SEA) to the time of the blood collection for

dioxin. If a participant had measurements at more than one point in time, the measurement closest to the time of duty in SEA was used. This exponential elimination law is termed "first-order elimination."

The first-order elimination assumption is equivalent to assuming a one-compartment model for dioxin distribution within the body. While a multicompartment model incorporating body composition and dioxin binding to tissue receptors would provide a detailed description of dioxin concentrations in different compartments, published multicompartment models for dioxin distribution within the body predict first-order elimination of dioxin, overwhelmingly because of fecal elimination (10).

The lipid-weight concentration of 1987 dioxin, expressed in ppt (11, 12), is a derived quantity calculated from the formula $W_{ppt} = W_{ppq} \cdot 102.6/W_{lipid}$, where W_{ppt} is the lipid-weight 1987 concentration, W_{ppq} (weight in parts per quadrillion) is the actual whole weight of dioxin in the sample in femtograms, 102.6 corrects for the average density of serum, and W_{lipid} is the total lipid weight of the sample (10).

The relation between the serum lipid-weight concentration of dioxin and lipid-weight concentrations in adipose tissue is a subject of continuing research. The correlation between the serum lipid-weight concentration and adipose tissue lipid-weight concentration of dioxin has been observed by Patterson et al. to be 0.98 in 50 persons from Missouri (13). Using the same data, Patterson et al. calculated the partitioning ratio of dioxin between adipose tissue and serum on a lipid-weight basis as 1.09 (95% confidence interval: [0.97,1.21]). On the basis of these data, a one-to-one partitioning ratio of dioxin between lipids in adipose tissue and the lipids in serum could not be excluded. Measurements of dioxin in adipose tissue generally have been accepted as representing the body burden concentration of dioxin. The high correlation between serum dioxin levels and adipose tissue dioxin levels in the Patterson et al. study suggests that serum dioxin is also a valid measurement of dioxin body burden.

The 1987 dioxin is considered a proxy exposure metric for exposures to dioxin-contaminated phenoxy herbicides (such as Agent Orange) because direct measures of exposure to these herbicides were not available. The elimination rate of dioxin is known to vary across individuals due to obesity and, perhaps, other unmeasured factors (7). Among Ranch Hand veterans with multiple repeated dioxin measurements, the dioxin elimination rate was inversely related to body fat; heavier individuals had a smaller elimination rate and a longer dioxin half-life than lean individuals (7). A statistical model relating dioxin elimination and body fat was not available at this writing. To account for the variation in the dioxin elimination rate with body fat, all statistical analyses based on Models 2 and 3 were adjusted for the body mass index at the time of the blood measurement of dioxin. The adequacy of this adjustment is not known.

7.2.2.2   *Model 2: Health Versus Initial Dioxin in Ranch Hands*

The relation between the estimated dioxin level at the time of exposure, termed "initial dioxin," and health was assessed in Ranch Hands using the statistical model described in Table 7-2. Statistical analyses based on this model were termed "Model 2" in the assessment of the clinical areas. In this statistical model, an initial dioxin level was estimated for a Ranch Hand from a 1987 lipid-adjusted dioxin measure, the length of time between the end of the veteran's last qualifying tour of duty in SEA and the date of the blood collection for the dioxin measurement , and an estimated half-life of 7.6 years. Model 2 is the same model that was used for the 1997 follow-up examination report (5), except that a dioxin half-life of 8.7 years was used for that report. From studies conducted by the Air Force, body mass index at the time of the blood measurement of dioxin appeared to be related to the dioxin half-life for a participant (7). Hence, a body mass index measure was included in this statistical model as a covariate. The adequacy of this adjustment is unknown. Model 2 differs from Model 1 in that the estimate of exposure in Model 1 (group: Ranch Hand, Comparison) was not dependent on extrapolation to an earlier date.

Table 7-2 describes Model 2 and also includes assumptions, advantages, and disadvantages of this model for a continuously distributed health variable, y. The statistical model presented in Table 7-2 is unadjusted for any additional risk factors, but extension to an adjusted model is straightforward.

Table 7-2. Model 2: Assessing Health Versus Initial Dioxin in Ranch Hands: Assumptions, Advantages, and Disadvantages

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Model 2: $y = b_0 + b_1\log_2(I) + b_2BMI + e$

where

y	=	health variable
b_0	=	intercept of the y-axis in the statistical model
b_1, b_2	=	slope parameters in the statistical model, corresponding to the variables $\log_2(I)$ and BMI, respectively
I	=	extrapolated initial dose, assuming first-order elimination, $I = 4+(C-4) \cdot \exp(\log(2) \cdot t/h)$, where 4 ppt is considered the median background level of lipid-adjusted dioxin; t = length of time between the time of duty in SEA and the date of the blood measurement of dioxin in 1987, 1992, 1997, or 2002; C = lipid-adjusted dioxin, determined in 1987, 1992, 1997, or 2002; and h = dioxin half-life in Ranch Hands assuming first-order elimination (7.6 years assumed for analysis)
BMI	=	body mass index at the time of the blood measurement of dioxin, calculated as weight/(height)^2 (14), where the weight is measured in kilograms and the height is measured in meters
e	=	zero mean error.

Assumptions: Ranch Hands received a single dioxin dose in Vietnam and background exposure thereafter.

Ranch Hands experienced first-order dioxin elimination.

The error variance does not change with health status or initial dioxin dose.

Advantages: Easily interpretable.

Uses the estimated initial dioxin dose, based on the 1987 value and a first-order model.

Most efficient if first-order elimination and half-life are valid and y is linearly related to $\log_2(I)$. The logarithm (base 2) of initial dioxin presents the dioxin data as a more symmetric distribution than the distribution of initial dioxin in its original units. In addition, the relative risk based on the logarithm (base 2) of initial dioxin is more meaningful than on the original scale (i.e., a doubling of initial dioxin rather than a 1 ppt increase in dioxin).

Disadvantages: Results are biased if first-order elimination or constant half-life assumptions are not valid.

The assumption that Ranch Hands received a single dioxin dose in Vietnam and background exposure thereafter is a simplification of an unknown and most likely complex exposure scenario. The assumption that Ranch Hands experienced first-order dioxin elimination is an approximation. A combined pharmacokinetic analysis of dioxin elimination in Ranch Hands and victims of the Seveso industrial accident (15) suggests that dioxin elimination is not first order and follows an approximate biphasic model, with fast elimination soon after (acute) exposure followed by slower elimination. The first-order model used in this study does not account for biphasic elimination. The same data (15), however, does

suggest that the first-order estimate of the initial dose is at least reasonable. Other more complicated nonlinear physiologically based pharmacokinetic models involving dose-dependence, body mass index, changes in body mass index and age are under development but were not ready for application in this report (16). Current data suggest that the dioxin elimination rate varies inversely with body mass index; heavier individuals have a smaller elimination rate and increased half-life relative to leaner individuals. Account of the dependence of the elimination rate on body mass index was made by adjusting all Model 2 and Model 3 analyses for the body mass index at the time of the blood measurement of dioxin. The adequacy of this adjustment is unknown.

Model 2 analyses were performed on Ranch Hands who had lipid-adjusted dioxin levels greater than 10 ppt at either the 1987, 1992, 1997, or 2002 physical examinations. The value 10 ppt corresponds to the approximate 98th percentile of the Comparison lipid-adjusted dioxin distribution. Based on this Comparison dioxin distribution, it was believed that participants with greater than 10 ppt lipid-adjusted dioxin were definitely exposed. It was not known whether Ranch Hands with dioxin burdens at or below 10 ppt were exposed and their body burdens had decreased to these levels since their time of duty in SEA, or whether they were not exposed at all during their time of duty in SEA. Lipid-adjusted dioxin levels less than 10 ppt were subsequently called "background" levels.

7.2.2.3   *Model 3: Health Versus Dioxin in Ranch Hands and Comparisons*

An assessment of the health consequences of dioxin above background levels was carried out with a statistical model that was applied to both Ranch Hand and Comparison data. This model assessed health versus dioxin body burden categorized into four levels, given below:

- Comparisons—All Comparisons, regardless of lipid-adjusted dioxin level

- Background—Ranch Hands with up to 10 ppt lipid-adjusted dioxin

- Low—Ranch Hands with more than 10 ppt lipid-adjusted dioxin but at most 118 ppt estimated initial dioxin

- High—Ranch Hands with more than 10 ppt lipid-adjusted dioxin and more than 118 ppt estimated initial dioxin.

Statistical analyses based on this model were termed "Model 3" in the assessment of the clinical outcomes. The cutpoint for the low and high Ranch Hand categories, of approximately equal size, was the median estimated initial dioxin level (118 ppt) of the Ranch Hands with more than 10 ppt lipid-adjusted dioxin. Note that the subset of Ranch Hands in the low and high dioxin categories combined is the same subset of Ranch Hands that are used in Model 2. The value of 118 ppt was revised from the value used for the 1997 follow-up examination (94 ppt) based on the updated 7.6-year half-life estimate and the cohort undergoing physical examinations for the 2002 physical examination. In this statistical model, an initial dioxin level (the same one used in Model 2) was estimated for a Ranch Hand from a 1987 lipid-weight dioxin measure, the length of time between the time of duty in SEA and the date of the blood collection for the dioxin measurement, and an estimated half-life of 7.6 years. From studies conducted by the Air Force, body mass index at the time of the blood measurement of dioxin appeared to be related to the dioxin half-life for a participant (7). Hence, a body mass index measure was included in this statistical model as a covariate. Using this body mass index in Model 3 for all Comparisons and Ranch Hands with dioxin measurements allowed body mass index to act as a potential risk factor and as an adjusting variable to explain half-life differences. The adequacy of this adjustment is unknown. It is

also unknown whether there were any individuals in the Background category who had an initial dioxin dose greater than 10 ppt and should have in fact been classified to the low or high dioxin category.

For a continuously distributed health variable, y, for example, the mean values of y within the background, low, high, and the low and high categories combined were contrasted with the mean values of y within the Comparison category. For a continuously distributed variable, the mean value of y for the low and high categories combined was calculated as a weighted average of the low dioxin and the high dioxin category means, with weights based on the sample size in each of these categories. For a discrete variable, the percentage of abnormal values for the low and high categories combined was calculated as a weighted average of the percentage abnormal in the low dioxin and the high dioxin categories, with weights based on the sample size in each of these categories. Table 7-3 shows this statistical model and the assumptions, advantages, and disadvantages for the unadjusted analysis of a continuous variable; extension to an adjusted model is straightforward. It should be noted that this statistical model is considered the "full model" in statistical terms and the coefficients b_0, b_1, b_2, b_3, and b_4 are not estimable. Reparameterization must be performed to estimate a linear combination of these coefficients.

Table 7-3. Model 3: Assessing Health Versus Categorized Dioxin in Ranch Hands and Comparisons: Assumptions, Advantages, and Disadvantages

Model 3: $y = b_0 + b_1I_1 + b_2I_2 + b_3I_3 + b_4I_4 + b_5BMI + e$
where
$\quad y$ = health variable
$\quad b_0$ = intercept of the y-axis in the statistical model
$\quad b_1, b_2, b_3, b_4, b_5$ = slope parameters in the statistical model, corresponding to the variables I_1, I_2, I_3, I_4, and BMI, respectively
$\quad I_1$ = indicator variable for categorized dioxin; $I_1 = 1$ if participant is a Comparison, $I_1 = 0$ if participant is not a Comparison
$\quad I_2$ = indicator variable for categorized dioxin; $I_2 = 1$ if participant is in background dioxin category, $I_2 = 0$ if participant is not in background dioxin category
$\quad I_3$ = indicator variable for categorized dioxin; $I_3 = 1$ if participant is in low dioxin category, $I_3 = 0$ if participant is not in low dioxin category
$\quad I_4$ = indicator variable for categorized dioxin; $I_4 = 1$ if participant is in high dioxin category, $I_4 = 0$ if participant is not in high dioxin category
$\quad BMI$ = body mass index at the time of the blood measurement of dioxin, calculated as weight/(height)^2 (14), where the weight is measured in kilograms and the height is measured in meters
$\quad e$ = zero mean error.
Assumptions: Dioxin body burden is eliminated following a first-order model.
The error variance does not change with categorized dioxin body burden.
Advantages: Initial dioxin is probably a better measure for determining low and high exposure than current or recent lipid-adjusted dioxin measurements.
Less dependent on the accuracy of the estimation algorithm for determining initial dioxin than Model 2.

Disadvantages:	Makes no use of prior belief that some Ranch Hands received an unusually large dioxin dose in Vietnam; all Ranch Hands with high dioxin levels are treated similarly.
	"Background" Ranch Hand category is probably a mixture of exposed and unexposed Ranch Hands. Analysis may be biased toward the null hypothesis of no dioxin effect.
	"Low" and "high" Ranch Hand categories are based on the initial dioxin model, which is based on valid half-life and first-order dioxin elimination. Bias is possible if model is incorrect. Also, a conditional null hypothesis is tested using these categories ("Is there a dioxin effect, given a specified level of exposure?").

An assumption of Model 3 is that dioxin is eliminated following a first-order model. As in Model 2, the adequacy of the first-order model can be questioned. The use of a common elimination rate to determine the cutpoint separating the low and high dioxin categories may induce misclassification because current data suggests that the rate is not constant and varies inversely with body mass index. The body mass index at the time of the blood measurement of dioxin was included in Models 2 and 3 to account for this variation, but the adequacy of this adjustment is unknown. Model 3 loses statistical power by collapsing the continuously distributed dioxin measure to a discrete measure.

A disadvantage of Model 3 is that it fails to give sufficient weight to Ranch Hands with very high doses. Another disadvantage of Model 3 is that the contrast between the Background category and Comparisons is not directly interpretable because the exposure status of individuals in the Background category is unknown. This fact was highlighted in the 1987 report by naming this category the "Unknown" category. Since 1992, the category has been named the "Background" category to simply reflect the dioxin cutpoint of 10 ppt. Another disadvantage is that some Comparisons were employed by U.S. industries, received substantial dioxin doses, are experiencing first-order elimination, and have dioxin pharmacokinetics and associations between dioxin and health.

7.2.2.4 *Model 4: Health Versus 1987 Dioxin in Ranch Hands*

The relation between 1987 dioxin and health was assessed using the statistical model described in Table 7-4. This measure of dioxin is termed "1987 dioxin" because most Ranch Hands were assayed for dioxin initially at the 1987 follow-up examination. This table also describes the assumptions, advantages, and disadvantages for the unadjusted analysis of a continuously distributed health variable, y.

Ranch Hands with a dioxin measurement may have had their blood collected at the pilot study in April 1987, at the 1987 physical examination, at the 1992 physical examination, at the 1997 physical examination, or at the 2002 physical examination. If an individual had measurements at more than one of these points in time, the measurement closest to the time of duty in SEA was used. If only a 1992 serum dioxin measurement was available, the level was extrapolated to the date of the 1987 physical examination. The model

$$C_{1987} = 4+(C_{1992}-4) \bullet \exp(rt)$$

was used for extrapolation of lipid-adjusted dioxin to 1987 levels (C_{1987}), where C_{1992} is the lipid-adjusted dioxin level in 1992, 4 ppt is considered the median background level for lipid-adjusted dioxin, $r = \log(2)/h$ is the elimination rate, h is the estimated half-life (7.6 years) of dioxin, and t is the length of time between the physical examination in 1987 and the physical examination in 1992. This model was

used only if the lipid-adjusted dioxin level in 1992 was greater than 10 ppt; otherwise, the 1992 measurement was used. A similar strategy was used for participants who had only a 1997 or a 2002 serum dioxin measurement.

The estimate of exposure in Model 4 (1987 dioxin) was based on extrapolation to the date of the 1987 physical examination for only a small percentage (3.5%) of Ranch Hands. Most measurements were based on 1987 dioxin measurements and extrapolation to 1987 levels was not needed for these measurements. Therefore, few of the 1987 dioxin values were estimated using the half-life of dioxin, which is dependent on the body mass index of the participant. Consequently, body mass index at the time of the blood measurement of dioxin was not used as a covariate in Model 4, which was different from the strategy used for Models 2 and 3.

1987 dioxin results below the limit of detection were calculated as the limit of detection divided by the square root of 2 (17). Dioxin results below the limit of quantitation were calculated as the limit of quantitation divided by the square root of 2 (17).

The relation between current health and dioxin was assessed using a statistical model, termed "Model 4," with lipid-adjusted 1987 dioxin as the estimate of exposure. Model 4 used the logarithm (base 2) of lipid-adjusted 1987 dioxin, as described in Table 7-4.

Table 7-4. Model 4: Assessing Health Versus 1987 Dioxin in Ranch Hands: Assumptions, Advantages, and Disadvantages

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Model 4: $y = b_0 + b_1\log_2(W_{ppt}) + e$

where

y = health variable

b_0 = intercept of the y-axis in the statistical model

b_1 = slope parameter in the statistical model, corresponding to the variable $\log_2(W_{ppt})$

W_{ppt} = lipid-adjusted 1987 dioxin = $W_{ppq} \cdot 102.6/W_{lipid}$, where W_{ppq} = whole weight of 1987 dioxin in the sample in femtograms (102.6 corrects for the average density of serum) and W_{lipid} = total lipid weight of the sample

e = zero mean error.

Assumptions: Ranch Hands received a single dioxin dose in Vietnam and background exposure thereafter.

The error variance does not change with health status or 1987 dioxin.

Advantages: Uses the dioxin measurement.

The logarithm (base 2) of (1987 dioxin) presents the dioxin data as a more symmetric distribution than the distribution of 1987 dioxin in its original units. In addition, the relative risk based on the logarithm (base 2) of (1987 dioxin) is more meaningful than on the original scale (i.e., a doubling of 1987 dioxin, rather than a 1 ppt increase in dioxin).

Disadvantages: 1987 dioxin may not be a good surrogate for exposure if elimination rate differs among individuals.

Individuals with measurements in 1992 only or 1997 only or 2002 only are extrapolated to 1987, and variation is increased with estimation using a first-order elimination model.

As in the other statistical models, the assumption that Ranch Hands received a single dioxin dose in Vietnam is a simplification of a complex and unknown exposure scenario.

The advantage that Model 4 uses the dioxin measurement is counterbalanced by the disadvantage that dioxin measure may not reflect the initial dose received by Ranch Hand veterans in Vietnam because the elimination rate appears to vary with body fat.

7.3   ANALYSIS METHODOLOGIES

7.3.1   Methods for Analyzing Continuous and Discrete Variables

For analyses of continuous dependent variables, the general linear models approach was used for applying such techniques as simple and multiple linear regression, analysis of variance, and analysis of covariance. This approach permitted model fitting of the dependent variable as a function of group or dioxin and specified covariates. Continuous dependent variables were examined to ensure that assumptions underlying appropriate statistical methods were met. Transformations (e.g., square root, logarithmic) were used to enhance normality for specific continuous health variables. A further discussion of general linear models and other methods used for the statistical analyses in this report are presented in Table 7-5.

For these continuous analyses, the SAS[®1] general linear models analysis (PROC GLM) (18) was used. After a statistical model was fitted, tests of significance for a group or dioxin effect were developed. Associations with a p-value less than or equal to 0.05 were described as significant.

The SAS[®] procedures PHREG and LIFETEST (18) were used for the time to diabetes onset variable in the endocrinology clinical assessment (see Sections 18.2.2.1.6 and 18.2.2.1.7 in Chapter 18, Endocrinology Assessment). Statistical methods used to analyze measures of this type can be implemented using a proportional hazards model (19). Table 7-5 presents a further discussion of the proportional hazards model.

For dichotomous discrete dependent variables, logistic regression was performed using SAS[®] PROC GENMOD (18). For dependent variables with more than two categories, polytomous logistic regression was performed using SAS[®] PROC CATMOD (18). Parameter estimation and model selection for polytomous logistic regression and ordinary logistic regression are similar. Both forms of regression use the maximum likelihood principle to obtain parameter estimates. For a model with k parameters for two equations, 2k parameters are estimated, k for each logit function. If ordinary logistic regression is applied twice (e.g., once for abnormal low versus normal and then for abnormal high versus normal), 2k parameters are estimated; however, ordinary logistic regression maximizes two likelihood equations, each with k parameters, while polytomous logistic regression estimates all 2k parameters simultaneously with one likelihood equation. Polytomous logistic regression also can be used for dependent variables that have more than three levels and require more than two contrasts with a normal category. A further discussion of logistic regression and polytomous logistic regression is found in Table 7-5.

A chi-square statistic, adjusted for the continuity of the chi-square distribution, was used when a test of the relative frequency of abnormal measurements between Ranch Hands and Comparisons was performed, and the relative frequency of either the Ranch Hand or the Comparison group was zero. This test statistic yields p-values approximately equal to Fisher's exact test (20) for a two-sided alternative hypothesis.

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Table 7-5. Summary of Statistical Procedures

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Chi-Square Contingency Table Test

The chi-square test of independence (20) is calculated for a contingency table by the following formula:

$$\chi^2 = \sum \frac{(f_O - f_E)^2}{f_E}$$

where the sum is taken over all cells of the contingency table and

f_O = observed frequency in a cell

f_E = expected frequency under the hypothesis of independence.

Large values indicate deviations from the null hypothesis and are tested for significance by comparing the calculated χ^2 to the tables of the chi-square distribution.

For 2x2 tables, the chi-square statistic above can be adjusted for the continuity of the χ^2 distribution. This test statistic yields p-values approximately equal to Fisher's exact test (20) for a two-sided alternative and is as follows:

$$\chi^2 = \sum \frac{\max(0,(|f_O - f_E| - \frac{1}{2}))^2}{f_E} \; .$$

Correlation Coefficient (Pearson's Product-Moment)

The population correlation coefficient ρ (21) measures the strength of the linear relation between two random variables X and Y. A commonly used sample-based estimate of this correlation coefficient is

$$\rho = \frac{\sum(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\left[\sum(x_i - \bar{x})^2 \sum (y_i - \bar{y})^2\right]}}$$

where the sum is taken over all (x, y) pairs in the sample. A student's t-test based on this estimator is used to test for a significant correlation between the two random variables of interest.

General Linear Models Analysis

The form of the general linear model (21) for two independent variables is

$$Y = \alpha + \beta_1 X_1 + \beta_2 X_2 + \varepsilon$$

where

Y	=	dependent variable (continuous)
α	=	level of Y at $X_1 = 0$ and $X_2 = 0$ (i.e., the intercept)
X_1, X_2	=	measured value of the first and second independent variables, respectively, which may be continuous or discrete (e.g., group status and age)
β_1, β_2	=	coefficient indicating linear association between Y and X_1, Y and X_2, respectively; each coefficient reflects the effect on the model of the corresponding independent variable adjusted for the effect of the other independent variable
ε	=	error term.

This statistical model assumes that the error terms are independent and normally distributed with a mean of 0 and a constant variance. Extension to more than two independent variables is immediate. Simple linear regression, multiple linear regression, analysis of variance, and analysis of covariance are all examples of a general linear models analysis.

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Table 7-5. Summary of Statistical Procedures (Continued)

Logistic Regression Analysis

The logistic regression model (22) enables a dichotomous dependent variable to be modeled in a regression framework with continuous and discrete independent variables. For two risk factors, such as dioxin and age, the logistic regression model is

$$\text{logit } P = \alpha + \beta_1 X_1 + \beta_2 X_2 + \varepsilon$$

where

P	=	probability of disease for an individual with risk factors X_1 and X_2
logit P	=	ln $(P/(1-P))$ (i.e., the log odds for disease)
X_1	=	first risk factor (e.g., dioxin)
X_2	=	second risk factor (e.g., age).

The parameters are interpreted as follows:

α	=	log odds for the disease when $X_1 = 0$ and $X_2 = 0$
β_1	=	coefficient indicating the dioxin effect adjusted for age
β_2	=	coefficient indicating the age effect adjusted for dioxin
ε	=	error term.

For a dichotomous measure, the term $\exp(\beta_1)$ equals the adjusted odds ratio of abnormal versus normal for Ranch Hands ($X_1 = 1$) compared to Comparisons ($X_1 = 0$). If the probability of being abnormal is small compared to being normal for both the Ranch Hand and Comparison groups, the odds ratio is approximately equal to the relative risk of being abnormal between the two groups. If X_1 is a continuous covariate, $\exp(\beta_1)$ represents the adjusted odds ratio of outcome 1 versus outcome 0 for a unit increase in X_1. If the risk factor is expressed in logarithmic (base 2) form, $\exp(\beta_1)$ reflects the adjusted odds ratio for a twofold increase in the risk factor.

Polytomous Logistic Regression Analysis

Polytomous logistic regression (22, 23) allows a categorical dependent variable with more than two outcomes to be modeled in a regression environment with continuous and discrete independent variables. For polytomous logistic regression, the model equation depends on the scale of the dependent variable. This discussion focuses on nominal scaled dependent variables.

Suppose Y is a nominal scaled dependent variable with three outcomes labeled 0, 1, or 2 (normal, low, or high). Polytomous logistic regression models two logit functions, one for Y = 1 versus Y = 0 and the other for Y = 2 versus Y = 0. The zero outcome for Y is called the reference category. To model Y with two covariates such as group status and age, the polytomous regression model would be

$$\text{logit } P_1 = \alpha_1 + \beta_{1(1)} X_1 + \beta_{1(2)} X_2 + \varepsilon_1$$

$$\text{logit } P_2 = \alpha_2 + \beta_{2(1)} X_1 + \beta_{2(2)} X_2 + \varepsilon_2$$

where

P_i	=	probability that Y = i (outcome i) with covariates X_1 and X_2, i = 0, 1, 2
logit P_i	=	ln (P_i/P_0) (i.e., the log odds of outcome i versus outcome 0, i = 1, 2)
X_1	=	first effect (e.g., group status)
X_2	=	second effect (e.g., age).

Table 7-5. Summary of Statistical Procedures (Continued)

Polytomous Logistic Regression Analysis (continued)

The parameters are interpreted as follows:

α_i = log odds of outcome i versus outcome 0 when $X_1 = 0$ and $X_2 = 0$, i = 1, 2

$\beta_{i(1)}$ = coefficient indicating the group status effect on the logit P_i, adjusted for age; i = 1, 2

$\beta_{i(2)}$ = coefficient indicating the age effect on the logit P_i, adjusted for group status; i = 1, 2

ε_i = error term for logit P_i, i = 1, 2.

This model assumes independent multinomial sampling.

Because the interpretation of each logistic modeling function is similar, consider the logit P_1 and suppose X_1 is a binary covariate ($X_1 = 1$ for Ranch Hands or $X_1 = 0$ for Comparisons). The term $\exp(\beta_{1(1)})$ equals the adjusted odds ratio of low versus normal for Ranch Hands ($X_1 = 1$) compared to Comparisons ($X_1 = 0$). If the probability of being low is small compared to being normal for both the Ranch Hand and Comparison groups, the odds ratio of low versus normal is approximately equal to the relative risk of being low between the two groups. If X_1 is a continuous covariate, $\exp(\beta_{1(1)})$ represents the adjusted odds ratio of outcome 1 versus outcome 0 for a unit increase in X_1.

Proportional Hazards Model

The Cox proportional hazards model (19) permits regression analysis of censored survival data and explains the effect of explanatory variables, or risk factors, on survival times. A proportional hazards model allows a nonconstant hazard rate, h(t) (e.g., rate at which diabetes is developed, which can vary with time), to be modeled as a function of either discrete or continuous risk factors. The proportional hazards model makes the assumption that the hazard functions in the cohorts of interest remain proportional to each other across time, and so the ratio of the hazard function in the groups is independent of time. The natural logarithm of the ratio of the hazard functions can be expressed as a linear combination of the risk factors.

Using the example of time to diabetes onset, for those participants who have developed diabetes, time to onset is defined as the time from the end of the participant's last qualifying tour to the date of diagnosis of diabetes. This time is known as the event time. If a participant has not developed diabetes, the time from the end of the participant's last qualifying tour to the date of the 2002 physical examination is known as the censoring time. The proportional hazards model accounts for both event times and censoring times to calculate the hazard ratio.

The parameters of the proportional hazards model can be estimated by partial likelihood methodology (24). These computations are performed using SAS® PROC PHREG (18), which accounts for censored survival times. PROC PHREG provides estimates, standard errors, and p-values from a chi-squared test on the parameter associated with each risk factor in the model. These statistics are used to test the significance of group (Model 1) or estimates of dioxin exposure (Models 2, 3, and 4) in the unadjusted and adjusted models.

For the example of time to diabetes onset, the summary statistic provided in this report is the 10th percentile of the hazard function. Because approximately 20 percent of the participants at the 2002 follow-up examination are diabetic, the 10th percentile is being used in this report to represent an estimate of the approximate median time to diabetes onset. Percentile estimates can be made for different cohorts, such as group, as given in Table 18-9(a) (Ranch Hand, Comparison), or a covariate such as race (Black, non-Black), as given in Appendix Table F-10. This observed time represents an estimate of the number of years that have elapsed since the end of the last qualifying tour until 10 percent of participants in the cohort of interest were diagnosed as diabetic.

Table 7-5. Summary of Statistical Procedures (Continued)

Proportional Hazards Model (continued)
In general, for the time to onset of a condition, the pth percentile is defined by the time period t such that p percent of the observations in the data have been diagnosed with the condition on or before the time period t. That is, for a random variable T, P(T≤t)=0.10. The 10th percentile of time to onset of diabetes was estimated using the SAS® procedure PROC LIFETEST (18). PROC LIFETEST computes nonparametric estimates of the survivor function via the Kaplan-Meier product-limit estimation procedure (25), where the survivor function is the probability that a participant has not developed diabetes by time t.

7.4 FACTORS DETERMINING THE STATISTICAL ANALYSIS METHOD

For a specified questionnaire-based or clinical measurement determined from the physical or laboratory examination, the selection of an analytical method depended on each of the following:

- Dependent Variable Form: Continuous or discrete

- Exposure Estimate and Analysis Cohort:

    o Model 1: Group—All Ranch Hands and Comparisons

    o Model 2: Initial dioxin—Ranch Hands having a dioxin body burden of greater than 10 ppt of lipid-adjusted dioxin, based on 1987 dioxin levels as defined in Section 7.2.2.4

    o Model 3: Categorized dioxin—Comparisons and all Ranch Hands with a lipid-adjusted dioxin measurement

    o Model 4: 1987 dioxin—All Ranch Hands with a lipid-adjusted dioxin measurement

- Analysis Type: Unadjusted or adjusted.

Table 7-6 specifies 16 separate analysis types based on dependent variable form, exposure estimate, analysis cohort, and analysis type. For each of the 16 types, the statistical method is specified. For example, linear regression models were used for adjusted analyses of initial dioxin for continuous dependent variables.

Table 7-6. Summary of Statistical Analysis Situations by Dependent Variable Form, Exposure Estimate, Analysis Cohort, and Analysis Type

Exposure Estimate	Analysis Cohort	Analysis Type	Statistical Methods	Independent Variables
Continuous				
Model 1: Group (Ranch Hands vs. Comparisons)	All Ranch Hands and Comparisons	Unadjusted	Analysis of Variance	Group
		Adjusted	Analysis of Covariance	Group; Covariates

Table 7-6. *Summary of Statistical Analysis Situations by Dependent Variable Form, Exposure Estimate, Analysis Cohort, and Analysis Type (Continued)*

Exposure Estimate	Analysis Cohort	Analysis Type	Statistical Methods	Independent Variables
Model 2: Log_2 (Initial Dioxin)	Ranch Hands >10 ppt lipid-adjusted 1987 dioxin	Unadjusted	Linear Regression	Log_2 (Initial Dioxin); Body Mass Index at the Time of the Blood Measurement of Dioxin
		Adjusted	Linear Regression	Log_2 (Initial Dioxin); Body Mass Index at the Time of the Blood Measurement of Dioxin; Covariates
Model 3: Categorized Dioxin	All Ranch Hands with a lipid-adjusted dioxin measurement, all Comparisons	Unadjusted	Analysis of Covariance	DXCAT; Body Mass Index at the Time of the Blood Measurement of Dioxin
		Adjusted	Analysis of Covariance	DXCAT; Body Mass Index at the Time of the Blood Measurement of Dioxin; Covariates
Model 4: Log_2 (1987 Dioxin)	All Ranch Hands with a lipid-adjusted dioxin measurement	Unadjusted	Linear Regression	Log_2 (1987 Dioxin)
		Adjusted	Linear Regression	Log_2 (1987 Dioxin); Covariates
Discrete				
Model 1: Group (Ranch Hands vs. Comparisons)	All Ranch Hands and Comparisons	Unadjusted	Chi-Square Contingency Table, Logistic Regression	Group
		Adjusted	Logistic Regression	Group; Covariates
Model 2: Log_2 (Initial Dioxin)	Ranch Hands >10 ppt lipid-adjusted 1987 dioxin	Unadjusted	Logistic Regression	Log_2 (Initial Dioxin); Body Mass Index at the Time of the Blood Measurement of Dioxin
		Adjusted	Logistic Regression	Log_2 (Initial Dioxin); Body Mass Index at the Time of the Blood Measurement of Dioxin; Covariates
Model 3: Categorized Dioxin	All Ranch Hands with a lipid-adjusted dioxin measurement, all Comparisons	Unadjusted	Chi-Square Contingency Table; Logistic Regression	DXCAT; Body Mass Index at the Time of the Blood Measurement of Dioxin
		Adjusted	Logistic Regression	DXCAT; Body Mass Index at the Time of the Blood Measurement of Dioxin; Covariates
Model 4: Log_2 (1987 Dioxin)	All Ranch Hands with a lipid-adjusted dioxin measurement	Unadjusted	Logistic Regression	Log_2 (1987 Dioxin)
		Adjusted	Logistic Regression	Log_2 (1987 Dioxin); Covariates

Note: Log_2 (Initial Dioxin) = Logarithm (base 2) of estimated initial dioxin level.
        DXCAT = Categorized dioxin (incorporating group membership—three categories for Ranch Hands, one category for Comparisons).
        Log_2 (1987 Dioxin) = Logarithm (base 2) of 1987 dioxin level.

7.4.1   Modeling Strategy

In general, based on one of the adjusted analysis statistical models described in Table 7-6, a model for dependent variables was based on the exposure effect (group or dioxin) and medically relevant covariates, as identified in Chapters 9 through 20 for each clinical category. As described previously, body mass index at the time of the blood measurement of dioxin was included in Models 2 and 3 as a covariate because these statistical models depended on the estimated initial dioxin and the estimate appears to vary with body fat. The adequacy of the adjustment for the body mass index is unknown.

The general modeling strategy did not remove any covariates from the model; however, the modeling strategy for the adjusted analysis of dependent variables in certain clinical areas was modified as necessary because of the large number of covariates or sparse number of participants with abnormal measurements. Stepwise elimination of covariates was conducted to allow for proper estimation of model parameters. When this strategy of removing covariates was necessary, the covariates removed from (or retained in) a model for a given health endpoint and statistical model were specified in footnotes to the tables in Chapters 9 through 20.

For Chapter 12, Psychology Assessment, 55 participants did not provide information for current total household income. Most of these participants refused to answer this question. For Chapter 15, Cardiovascular Assessment, 52 participants did not provide information for family history of heart disease before age 45. Most of these participants did not know the answer to this question. In an attempt not to exclude a substantial number of participants in these two chapters, a limited version of a stepwise procedure was used. If current total household income or family history of heart disease before age 45 was not significant ($p>0.05$) in Chapters 12 and 15, respectively, for the adjusted analysis of a dependent variable for a particular model, the covariate was excluded from the analysis. Excluding current total household income and family history of heart disease from the statistical model, where appropriate, allowed the participants who did not provide information for these variables to be included in the analysis of the model and thus increased the sample size. The parameters of the statistical model were then re-estimated; the statistics from the re-estimated models were shown in the chapter tables. A footnote to the table specifies when current total household income or family history of heart disease before age 45 was deleted as a covariate.

7.5   STUDY LIMITATIONS, STRENGTHS, AND STATISTICAL POWER

This study was limited by the sample size (preventing the study of rare diseases), imperfect exposure metrics, and the possible existence of other confounding factors that we have not measured. Study strengths included complete record verification of all statistically analyzed health conditions, rigorous quality control, good compliance, complete population ascertainment, many years of follow-up, and adjustment for many known confounding factors.

Although many covariates were considered in this report, there are others that may be unknown and some that were measured but not used in this report. Some of the analyses in this report, therefore, may be biased due to lack of adjustment for an important confounding covariate. Recent studies of cancer in Ranch Hand veterans indicate that the calendar period and length of service in the Ranch Hand unit is an important covariate, for example, but this fact was discovered after the analytical plan for this report was already in place.

The study benefited from a two-tiered management structure based on separate but parallel program management and technical teams, an independently appointed and administered Advisory Committee, periodic review by the Institute of Medicine, and collaboration through interagency agreements between the Air Force and the Centers for Disease Control making the dioxin measurements possible. The

management structure, oversight, carefully managed funding and contracting and outstanding contractors all contributed to uniformly rigorous quality assurance, attention to detail, and timely task completion.

7.5.1　Power

A type I error is making a false conclusion that an association (group or dioxin effect) exists when there is no association. The other possible inference error, a type II error, is the failure to detect an association when one actually exists. The power of a statistical test is 1 minus the probability of a type II error. The power of the test is the probability that the test will reject the hypothesis of no group or dioxin effect when an effect does in fact exist.

The fixed size of the Ranch Hand cohort limits the ability of this study to detect some group or dioxin associations if they exist. This limitation is most obvious for specific types of cancer, such as soft tissue sarcoma and non-Hodgkin's lymphoma. These conditions are so uncommon that fewer than two cases were expected in this study, indicating that there is virtually no statistical power to detect low-to-moderate associations between dioxin and cancer. In an attempt to overcome the lack of power to detect group differences for specific types of systemic cancer, for example, all types of systemic cancer were combined into a single variable. It is still possible, however, that an increased risk could exist for a particularly rare type of cancer, allowing that increased risk to be missed in this study.

Table 7-7 and Appendix Tables E-1 through E-3 contain the approximate power at a significance level of 0.05 to detect specified relative risks for a given prevalence rate of a discrete dependent variable. Table 7-7 presents power calculations for Model 1 (group) and Appendix Tables E-1 through E-3 present power calculations for Model 2 (initial dioxin), Model 3 (categorized dioxin—low and high Ranch Hand dioxin categories combined versus Comparison contrast), and Model 4 (lipid-adjusted 1987 dioxin). Power calculations were performed using the logarithm (base 2) of dioxin in Models 2 and 4. Consequently, the relative risk is for a twofold increase in dioxin in Models 2 and 4. The power of a test for a discrete variable depends on the significance level, actual relative risk, prevalence of the condition, and the Ranch Hand and Comparison sample sizes (for Models 1 and 3) or the distribution of the dioxin data (for Models 2 and 4). As an example, Table 7-7 shows a power of 0.20 to detect a relative risk of 2.0 for a disease with a prevalence of 0.005. For a disease with a prevalence of 0.05, the power to detect a relative risk of 1.5 would be 0.50.

Table 7-7.　Approximate Power to Detect a Group Effect at a 5-Percent Level of Significance (Discrete Dependent Variable)

Prevalence of Condition	Relative Risk								
	1.10	1.20	1.30	1.40	1.50	1.75	2.00	10.00	20.00
0.005	0.05	0.06	0.07	0.08	0.10	0.14	0.20	0.91	0.97
0.01	0.05	0.07	0.09	0.12	0.15	0.24	0.34	1.00	1.00
0.02	0.06	0.09	0.13	0.18	0.24	0.42	0.59	1.00	1.00
0.03	0.06	0.10	0.17	0.25	0.34	0.57	0.76	1.00	1.00
0.04	0.07	0.12	0.21	0.31	0.42	0.69	0.86	1.00	1.00
0.05	0.07	0.14	0.24	0.37	0.50	0.78	0.92	1.00	1.00
0.10	0.10	0.22	0.41	0.61	0.77	0.96	1.00	1.00	1.00
0.15	0.11	0.30	0.54	0.75	0.89	0.99	1.00	1.00	1.00
0.20	0.13	0.36	0.63	0.84	0.95	1.00	1.00	1.00	1.00

Table 7-8 and Appendix Tables E-4 through E-6 provide the same information on power as Table 7-7 and Appendix Tables E-1 through E-3 for a continuous dependent variable at a significance level of 0.05. The power calculations are defined in terms of the coefficient of variation (100 times the standard deviation of the dependent variable divided by the mean of the dependent variable) and the proportion mean change. The coefficient of variation relates the spread of the data relative to the magnitude of the data. In general, the power of a test is greater when the coefficient of variation is smaller. Table 7-8 presents power calculations for Model 1 (group) and Appendix Tables E-4 through E-6 present power calculations for Model 2 (initial dioxin), Model 3 (categorized dioxin—low and high Ranch Hand dioxin categories combined versus Comparison contrast), and Model 4 (lipid-adjusted 1987 dioxin). Power calculations were performed using the logarithm (base 2) of dioxin in Models 2 and 4. Consequently, the relative risk is for a twofold increase in dioxin. The power of a test for a continuous variable depends on the significance level, actual difference in the true dependent variable means or slope of the dioxin coefficient, variation in the dependent variable data, sample size, and the distribution of the dioxin data if dioxin is the exposure estimate.

The proportion mean change in Table 7-8 and Appendix Table E-5 is defined as the difference in the true Ranch Hand and Comparison means, relative to the combined average of the two groups, assuming no transformation of the dependent variable. The proportion mean change in Appendix Tables E-4 and E-6 is defined as the change in the expected value (mean) of the dependent variable for a twofold increase in initial dioxin, relative to the dependent variable mean. The proportion mean change in Appendix Tables E-4 and E-6 corresponds mathematically to the slope of initial or 1987 dioxin divided by the dependent variable mean, assuming no transformation of the dependent variable. Analogous quantities can be derived based on transformed statistics. As an example, white blood cell (WBC) count (on the natural logarithm scale) for all participants has a coefficient of variation of approximately 15 percent. With this coefficient of variation, for the 777 Ranch Hands and 1,174 Comparisons in Model 1, the power is approximately 0.82 for detecting a 2-percent increase in the mean WBC count of Ranch Hands relative to the mean WBC count of Comparisons (mean change = 0.02).

Table 7-8. Approximate Power to Detect a Group Effect at a 5-Percent Level of Significance (Continuous Dependent Variable)

Mean Change	Coefficient of Variation ($100\sigma/\mu$)					
	5	10	15	25	50	75
0.005	0.58	0.19	0.11	0.07	0.06	0.05
0.01	0.99	0.58	0.30	0.14	0.07	0.06
0.02	1.00	0.99	0.82	0.41	0.14	0.09
0.03	1.00	1.00	0.99	0.74	0.25	0.14
0.04	1.00	1.00	1.00	0.93	0.41	0.21
0.05	1.00	1.00	1.00	0.99	0.58	0.30
0.10	1.00	1.00	1.00	1.00	0.99	0.82

In summary, this study has good power to detect relative risks of 2.0 or more with respect to diseases, such as heart disease and basal cell carcinoma, occurring at a prevalence of at least 5 percent in unexposed populations. In addition, the study size is sufficient to detect small mean shifts in the continuously distributed variables. The detection of significant mean shifts without a corresponding indication of increased Ranch Hand abnormalities or disease may be an artifact of multiple testing, could represent a subclinical effect, or could be of little or no medical importance.

7.6   EXPLANATION OF TABLES

This section explains the contents of the tables used to report the results of the analyses for continuous and discrete dependent variables (two levels and more than two levels). Selected tables from the General Health Assessment (Chapter 9) and the Hematology Assessment (Chapter 16) will be referenced throughout this discussion. The contents of each table depend on the form of the health status endpoint (i.e., whether the dependent variable under analysis is a continuous or discrete variable).

The results of the exposure analysis are displayed in subpanels within each table as specified in Table 7-9. The specification of the subpanels is applicable whether the dependent variable is continuous or discrete.

Table 7-9. Location of Table Results from Different Exposure Analysis Models

Model	Exposure Estimate	Analysis Cohort	Subpanel in Table	Type of Analysis
1	Group	All Ranch Hands and Comparisons	a	Unadjusted
			b	Adjusted
2	Initial Dioxin	Ranch Hands >10 ppt lipid-adjusted 1987 dioxin	c	Unadjusted
			d	Adjusted
3	Categorized Dioxin	All Ranch Hands with a lipid-adjusted dioxin measurement, all Comparisons	e	Unadjusted
			f	Adjusted
4	1987 Dioxin	All Ranch Hands with a lipid-adjusted dioxin measurement	g	Unadjusted
			h	Adjusted

7.6.1   Continuous Variables

Table 16-3 in the Hematology Assessment chapter presents an example of the results of the analysis when the dependent variable was continuous. Subpanels (a) and (b) show the results of unadjusted and adjusted Model 1 analyses that compared the Ranch Hand and Comparison means of a dependent variable. Contrasts between Ranch Hands and Comparisons also are presented within each military occupational category (i.e., officer, enlisted flyer, and enlisted groundcrew).

For the unadjusted analysis in subpanel (a), a sample size (n) and a mean are presented for all military occupational categories combined and separately for each occupational category. If the dependent variable was transformed for the analysis, the means of the transformed values were converted to the original scale and the column heading is footnoted. For each contrast of Ranch Hands versus Comparisons, the difference of means on the original scale and the associated 95-percent confidence interval are reported. The 95-percent confidence interval was constructed by adding and subtracting 1.96 multiplied by the standard error (for the upper and lower bounds, respectively) to the estimated mean. If the analysis was performed on a transformed scale, the 95-percent confidence interval on the differences of means is not presented and the column is footnoted. When presenting results from analyses of means based on log-transformed (or square root-transformed) data, means were converted back to original units. Conversion of the standard deviation from log units to original units is not recommended (26); therefore, confidence intervals for mean differences in original units are not presented when the variable is analyzed on the logarithmic or square root scale. A p-value also is reported to determine whether a difference in means on the scale used for analysis for a specified contrast was equal to zero. The confidence interval and p-value for each military occupational category were determined using analysis of variance techniques from a group-by-occupation interaction in the statistical model. The group-by-occupation interaction was used to determine the model coefficients and standard errors simultaneously for officers,

enlisted flyers, and enlisted groundcrew. The respective coefficients and standard errors from the group and group-by-interaction terms in the model, along with the covariances between the estimates, were combined as appropriate to construct the confidence intervals and p-values for the three military occupational strata.

For an adjusted Model 1 analysis, subpanel (b) includes a sample size, an adjusted mean, a difference of Ranch Hand and Comparison adjusted means on the original scale, the associated 95-percent confidence interval (if the analysis was performed on the original scale), and a p-value for each contrast. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information. The confidence interval and p-value for each military occupational category were determined using analysis of covariance techniques from a group-by-occupation interaction in the statistical model.

Subpanel (c) of Table 16-3 reports summary statistics from the analysis that assessed the association between the continuous dependent variable and initial dioxin (Model 2) without adjusting for covariate information. The sample size and mean of the dependent variable (transformed to the original units, if necessary) are presented for low, medium, and high categories of initial dioxin. The low, medium, and high categories were determined by dividing all Ranch Hands with initial dioxin estimates into three approximately equally sized categories based on their initial dioxin estimate. The numerical values defining these categories are specified in a table subpanel footnote. Means of the dependent variable, adjusted for body mass index at the time of the blood measurement of dioxin, also are presented for the low, medium, and high categories of initial dioxin. Based on a linear regression analysis adjusted for body mass index at the time of the blood measurement of dioxin, the coefficient of determination (R^2), the estimated slope, and its associated standard error are reported. If the dependent variable was transformed for the regression analysis, the transformation is identified in the footnote. The p-value associated with testing whether the slope was equal to zero also is presented. The summary statistics that are reported were based on initial dioxin divided into three categories, whereas the R^2, slope, standard error, and p-value were based on $\log_2$ (initial dioxin) in its continuous form.

Based on analyses that incorporate covariate information, subpanel (d) reports summary statistics from the analysis that assessed the association between the continuous dependent variable and initial dioxin (Model 2). Similar to the unadjusted analysis, a sample size and adjusted mean of the dependent variable (transformed to the original units, if necessary) are presented for low, medium, and high categories of initial dioxin. The numerical values defining these categories are specified in a table subpanel footnote. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information. Based on the multiple linear regression of the dependent variable on $\log_2$ (initial dioxin) and covariate effects, including body mass index at the time of the blood measurement of dioxin, the R^2, the adjusted slope for $\log_2$ (initial dioxin), and its associated standard error are reported. If the dependent variable was transformed for the regression analysis, the adjusted means, adjusted slope, and standard error are footnoted and the transformation is identified in the footnote. The p-value for testing whether the slope was equal to zero also is presented.

Subpanels (e) and (f) of Table 16-3 show the results of unadjusted and adjusted Model 3 analyses that contrasted the means of a continuous dependent variable for Ranch Hands with background, low, high, and low plus high dioxin levels with all Comparisons. The low and high Ranch Hand categories were determined by dividing all Ranch Hands with lipid-adjusted dioxin estimates greater than 10 ppt into two approximately equally sized categories based on their initial dioxin estimate. The note at the bottom of the table subpanels defines the dioxin categories. The low plus high Ranch Hand category is a combination of the low and high categories. The mean for the low plus high category is a weighted average (transformed to the original units, if necessary) of the low Ranch Hand and high Ranch Hand

category means on the scale used for transformation, where the weights were based on the low and high Ranch Hand category sample sizes. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information.

For the unadjusted analysis in subpanel (e), a sample size and dependent variable mean are presented for each category. If the dependent variable was transformed for the analysis, the means of the transformed values were converted to the original scale and the column heading is footnoted. The mean of the dependent variable adjusted for body mass index at the time of the blood measurement of dioxin also is presented for each dioxin category. For each individual contrast of the Ranch Hand category versus the Comparison category, the difference of means on the original scale and the associated 95-percent confidence interval are reported. If the analysis was performed on a transformed scale, the 95-percent confidence interval on the differences of means is not presented and the column is footnoted. A p-value also is reported to determine whether a difference in means for a specified contrast was equal to zero. The p-value was based on the difference of means on the scale used for analysis. The adjusted mean, confidence interval, and p-value for each contrast were determined from an analysis of covariance statistical model with adjustment for body mass index at the time of the blood measurement of dioxin.

For the adjusted analysis in subpanel (f), the table includes a sample size, an adjusted mean (adjusted for body mass index at the time of the blood measurement of dioxin and covariates), a difference in adjusted means on the original scale, and a 95-percent confidence interval on the difference in adjusted means (if the analysis was performed on the original scale). The p-value for testing whether the difference in adjusted means for a specified contrast was equal to zero also is presented.

Subpanel (g) of Table 16-3 reports summary statistics from Model 4 analyses, which assessed the association between the continuous dependent variable and 1987 dioxin without adjusting for covariate information. The sample size and mean of the dependent variable (transformed to the original units, if necessary) are presented for low, medium, and high categories of 1987 dioxin. The low, medium, and high categories were determined by dividing all Ranch Hands with 1987 dioxin levels into three approximately equally sized categories based on their 1987 dioxin measurement and are defined in a table subpanel footnote. Based on a linear regression of the dependent variable on $\log_2$ (1987 dioxin), the R^2, the estimated slope, and its associated standard error are reported for each model. If the dependent variable was transformed for the regression analysis, the means, slope, and standard error are footnoted and the transformation is identified in the footnote. The p-value associated with testing whether the slope was equal to zero also is presented.

Based on analyses that incorporate covariate information, subpanel (h) reports summary statistics for Model 4 analyses that assessed the association between the continuous dependent variable and 1987 dioxin. The sample size and adjusted mean of the dependent variable (transformed to the original units, if necessary) are presented for low, medium, and high categories of 1987 dioxin. The numerical values defining these categories are specified in a table subpanel footnote. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information. Based on the multiple linear regression of the dependent variable on $\log_2$ (1987 dioxin) and covariates, the R^2, the adjusted slope for $\log_2$ (1987 dioxin), and its associated standard error are reported for each model. If the dependent variable was transformed for the regression analysis, the adjusted means, adjusted slope, and standard error are footnoted and the transformation is identified in the footnote. The p-value for testing whether the slope was equal to zero also is presented.

7.6.2   Discrete Variables

7.6.2.1   *Discrete Variable with Two Categories*

Table 9-3 in the General Health Assessment chapter presents an example of the results of analysis when the dependent variable is discrete and dichotomous. Subpanels (a) and (b) display the results of unadjusted and adjusted Model 1 analyses that compared the percentage of Ranch Hands and Comparisons that were considered abnormal for the dependent variable of interest (the abnormal classification for self-perception of health in Table 9-3 is "fair or poor"). Contrasts between Ranch Hands and Comparisons also are presented within each military occupational category (i.e., officer, enlisted flyer, and enlisted groundcrew). For the unadjusted analysis in subpanel (a), a sample size and the number and percentage of participants considered abnormal are presented for each group within each military occupational category. For the contrasts of Ranch Hands versus Comparisons, an unadjusted relative risk, an associated 95-percent confidence interval on the relative risk, and a p-value for testing whether the risk was equal to 1.0 are presented. The normal distribution was used to calculate an approximate 95-percent confidence interval. Results for each military occupational category were determined from a group-by-occupation interaction that was included in the statistical model.

For the adjusted analysis of Model 1, as presented in subpanel (b), the table presents a sample size, an adjusted relative risk, a 95-percent confidence interval on the relative risk, and a p-value for testing whether the risk was equal to 1.0 for all military occupational categories combined and separately for each occupational category. The sample size, adjusted relative risk, confidence interval, and p-value were determined from a multiple logistic regression model that used the appropriate covariates for the clinical area and dependent variable of interest. Results for each military occupational category were determined from a group-by-occupation interaction that was included in the statistical model. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information.

Subpanel (c) of Table 9-3 reports summary statistics for analyses that assessed the association between the dependent variable and initial dioxin (Model 2) without adjusting for covariate information. Sample sizes are presented for low, medium, and high categories of initial dioxin. The numerical values defining these categories are specified in a table footnote. The number and percentage of Ranch Hands considered abnormal are presented for the low, medium, and high initial dioxin categories. Based on a logistic regression model, adjusted for body mass index at the time of the blood measurement of dioxin, an unadjusted relative risk and its 95-percent confidence interval are reported. The p-value associated with testing whether the relative risk was equal to 1.0 also is presented. The normal distribution was used to determine an approximate 95-percent confidence interval. The summary statistics that are reported were based on initial dioxin divided into three categories, whereas the relative risk, confidence interval, and p-value were based on $\log_2$ (initial dioxin) in its continuous form.

Subpanel (d) of Table 9-3 reports summary statistics for analyses that assessed the association between the discrete dependent variable and initial dioxin (Model 2), adjusted for body mass index at the time of the blood measurement of dioxin and covariate information. The sample size given is based on a multiple logistic regression of the discrete dependent variable on $\log_2$ (initial dioxin), body mass index at the time of the blood measurement of dioxin, and covariates. Total sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information. The adjusted relative risk for $\log_2$ (initial dioxin) and its associated 95-percent confidence interval are reported and are based on this multiple logistic regression model. The normal distribution was used to determine an approximate 95-percent confidence interval. The p-value for testing whether the relative risk was equal to 1.0 also is presented.

Subpanels (e) and (f) of Table 9-3 show the results of unadjusted and adjusted Model 3 analyses that contrasted Ranch Hands having background, low, high, and low plus high dioxin levels with all Comparisons. The percentage of participants that were considered abnormal for the dependent variable of interest was contrasted between the four categories of Ranch Hands and Comparisons. The low and high Ranch Hand categories were determined by dividing all Ranch Hands with lipid-adjusted dioxin estimates greater than 10 ppt into two approximately equally sized categories based on their initial dioxin estimate. The low plus high Ranch Hand category is a combination of the low and high Ranch Hand categories. The footnote at the bottom of the table subpanel defines the dioxin categories. The percentage of Ranch Hands in the low plus high category is a weighted average of the low Ranch Hand and high Ranch Hand category percentages, where the weights are based on the low category and high category sample sizes. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information.

For the Model 3 unadjusted analysis in subpanel (e), the sample size and the number and percentage of participants considered abnormal is presented for each dioxin category. For the individual contrasts of the Ranch Hand categories versus Comparisons, an unadjusted relative risk, a 95-percent confidence interval for the relative risk, and a p-value associated with testing whether the risk was equal to 1.0 are presented. The relative risk, confidence interval, and p-value were determined from a logistic regression model, adjusted for body mass index at the time of the blood measurement of dioxin. The normal distribution was used to determine an approximate 95-percent confidence interval.

For the Model 3 adjusted analysis, subpanel (f) of the table presents sample size, an adjusted relative risk, a 95-percent confidence interval for the relative risk, and a p-value associated with testing whether the risk was equal to 1.0 for the individual contrasts of the Ranch Hand categories with Comparisons. The relative risk, confidence interval, and p-value were determined from a logistic regression model, adjusted for body mass index at the time of the blood measurement of dioxin and covariates. The normal distribution was used to determine an approximate 95-percent confidence interval.

Subpanels (g) and (h) of Table 9-3 present summary statistics from Model 4, which assessed the association between the dependent variable and 1987 dioxin. For the unadjusted analysis in subpanel (g), the sample size and the number and percentage of participants considered abnormal is presented for each 1987 dioxin category. The low, medium, and high categories were determined by dividing all Ranch Hands with 1987 dioxin levels into three approximately equally sized categories. The numerical values defining these categories are specified in a table footnote. Based on a logistic regression model, an unadjusted relative risk and its 95-percent confidence interval are reported. The p-value associated with testing whether the relative risk was equal to 1.0 also is presented. The normal distribution was used to determine an approximate 95-percent confidence interval. The summary statistics are reported for 1987 dioxin divided into three categories, whereas the relative risk, confidence interval, and p-value were based on $\log_2$ (1987 dioxin) in its continuous form.

Incorporating covariate information, subpanel (h) reports summary statistics from analyses that assessed the association between the dichotomous dependent variable and 1987 dioxin. The sample size is presented for a multiple logistic regression of the discrete dependent variable on $\log_2$ (1987 dioxin) including covariates in the final adjusted model. Total sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information. Based on the multiple logistic regression model, the adjusted relative risk for $\log_2$ (1987 dioxin) and its associated 95-percent confidence interval are reported. The normal distribution was used to determine an approximate 95-percent confidence interval. The p-value for testing whether the relative risk was equal to 1.0 also is presented.

7.6.2.2   Discrete Variable with More Than Two Categories

Polytomous regression techniques were used to analyze discrete dependent variables having more than two levels (e.g., abnormal low, normal, abnormal high—see Table 16-4 in the Hematology Assessment chapter). Results were presented in a similar fashion to discrete variables with only two categories; however, the number and percentage of participants for each dependent variable category (including normal) are given. Therefore, the relative frequencies sum to 100 percent across the dependent variable categories and the number of participants in each of the dependent variable categories adds to the total number of participants in each exposure group or dioxin category. In addition, a relative risk, a 95-percent confidence interval, and a p-value were presented for each contrast with the normal level of the dependent variable (e.g., abnormal low versus normal and abnormal high versus normal).

In Table 16-4, subpanels (a) and (b) display the results of unadjusted and adjusted Model 1 analyses that compared Ranch Hands and Comparisons on the relative frequencies of each abnormal level for a specified discrete dependent variable. For example, the percentage of participants with an abnormally high red blood cell (RBC) count was contrasted to participants with a normal RBC count, and the percentage of participants with an abnormally low RBC count was contrasted to participants with a normal RBC count. Contrasts between Ranch Hands and Comparisons also are presented within each military occupational category (i.e., officer, enlisted flyer, and enlisted groundcrew). For the unadjusted analysis in subpanel (a), a sample size is presented for each exposure group (Ranch Hand, Comparison) across all military occupational categories and within each occupational category. For the contrasts of Ranch Hands versus Comparisons, an unadjusted relative risk, a 95-percent confidence interval for the relative risk, and a p-value associated with testing whether the risk was equal to 1.0 are presented for each contrast against the normal level of the dependent variable (e.g., abnormal low versus normal and abnormal high versus normal). The normal distribution was used to calculate an approximate 95-percent confidence interval. Results for each military occupational category were determined from the group-by-occupation interaction that was included in the statistical model.

For a Model 1 analysis adjusted for covariate information and shown in subpanel (b), the table presents an adjusted relative risk, a 95-percent confidence interval on the relative risk, and a p-value associated with testing whether the risk was equal to 1.0 for each military occupational category and each contrast. The normal distribution was used to calculate an approximate 95-percent confidence interval. Results for each military occupational category were determined from the group-by-occupation interaction that was included in the statistical model. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information.

Subpanels (c) and (d) of Table 16-4 summarize the unadjusted and adjusted Model 2 analyses relating initial dioxin to discrete dependent variables having more than two categories. Both unadjusted and adjusted analyses are adjusted for body mass index at the time of the blood measurement of dioxin. In subpanel (c), the sample size and the number and percentage of Ranch Hands in each category of the dependent variable are presented for each initial dioxin category (i.e., low, medium, and high initial dioxin), which are defined in a footnote to the subpanel. The relative risk, the 95-percent confidence interval for the relative risk, and the p-value associated with testing whether the risk was equal to 1.0 are presented for each abnormal level of the dependent variable (e.g., abnormal low versus normal and abnormal high versus normal). The summary statistics that are reported were based on initial dioxin divided into three categories, whereas the relative risk, confidence interval, and p-value were based on $\log_2$ (initial dioxin) in its continuous form.

In subpanel (d), after adjustment for covariate information, the sample size, the adjusted relative risk, the 95-percent confidence interval for the relative risk, and the p-value associated with testing whether the risk was equal to 1.0 are presented for each abnormal level of the dependent variable. Total sample sizes

for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information.

Subpanels (e) and (f) of Table 16-4 present unadjusted and adjusted Model 3 analyses of categorized dioxin versus a discrete dependent variable having more than two categories. Both unadjusted and adjusted analyses are adjusted for body mass index at the time of the blood measurement of dioxin. Results are presented in a similar fashion to the dichotomous analysis, except that contrasts other than abnormal versus normal are presented (e.g., abnormal high versus normal, along with abnormal low versus normal). For the unadjusted analysis, a sample size is presented for each dioxin category. The low plus high Ranch Hand category is a combination of the low and high Ranch Hand categories. The percentage of Ranch Hands in the low plus high category is a weighted average of the low Ranch Hand and high Ranch Hand category percentages, where the weights are based on the low category and high category sample sizes. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information.

The total sample size and the number and percentage of participants for each level of the dependent variable are presented for each dioxin category in subpanel (e). For each contrast of a Ranch Hand category versus the Comparison group, an unadjusted relative risk, a 95-percent confidence interval for the relative risk, and a p-value associated with testing whether the risk was equal to 1.0 are presented. These results are given for each contrast against the normal level of the dependent variable (e.g., abnormal low versus normal and abnormal high versus normal). For an adjusted Model 3 analysis in subpanel (f), the table presents sample sizes and an adjusted relative risk, a 95-percent confidence interval on the relative risk, and a p-value for each contrast of Ranch Hands versus Comparisons for each abnormal level of the dependent variable.

Unadjusted and adjusted analyses of discrete dependent variables with more than two categories were performed using 1987 dioxin in Model 4. In Table 16-4, summaries of the analyses are given in subpanels (g) and (h). Results are presented in a similar fashion to the dichotomous analysis, except that contrasts other than abnormal versus normal are presented (e.g., abnormal high versus normal, along with abnormal low versus normal). For the unadjusted analysis in subpanel (g), sample sizes are presented for each 1987 dioxin category (i.e., low, medium, and high 1987 dioxin). The number and percentage of Ranch Hands for each dependent variable category for each 1987 dioxin category are presented. An unadjusted relative risk, a 95-percent confidence interval on the relative risk, and an associated contrast p-value are reported for each abnormal level of the dependent variable (e.g., abnormal low versus normal and abnormal high versus normal). The summary statistics that are reported were based on 1987 dioxin divided into three categories, whereas the relative risk, confidence interval, and p-value were based on $\log_2$ (1987 dioxin) in its continuous form.

Adjusted analysis results in subpanel (h) include a total sample size and an adjusted relative risk, a 95-percent confidence interval on the relative risk, and an associated contrast p-value for each contrast of the dependent variable. Sample sizes for corresponding panels of unadjusted and adjusted analyses may differ because of missing covariate information.

REFERENCES

1. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline morbidity study results. NTIS: AD A 138 340. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

2. Lathrop, G.D., S.G. Machado, T.G. Karrison, W.D. Grubbs, W.F. Thomas, W.H. Wolfe, J.E. Michalek, J.C. Miner, and M.R. Peterson. 1987. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188 262. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

3. Thomas, W.F., W.D. Grubbs, T.G. Karrison, M.B. Lustik, R.H. Roegner, D.E. Williams, W.H. Wolfe, J.E. Michalek, J.C. Miner, and R.W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

4. Grubbs, W.D., W.H. Wolfe, J.E. Michalek, D.E. Williams, M.B. Lustik, A.S. Brockman, S.C. Henderson, F.R. Burnett, R.G. Land, D.J. Osborne, V.K. Rocconi, M.E. Schreiber, J.C. Miner, G.L. Henriksen, and J.A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final Report. 1992 followup examination results. NTIS: AD A 304 306, 304 308-316. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

5. Michalek, J.E., B.R. Burnham, H.E. Marden, Jr., J.N. Robinson, V.V. Elequin, J.C. Miner, R.W. Ogershok, W.K. Sneddon, W.D. Grubbs, B.C. Cooper, R.G. Land, V.K. Rocconi, M.E. Yeager, D.E. Williams, and M.E.B. Owens. 2000. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1997 follow-up examination results. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

6. Roegner, R.H., W.D. Grubbs, M.B. Lustik, A.S. Brockman, S.C. Henderson, D.E. Williams, W.H. Wolfe, J.E. Michalek, and J.C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

7. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57:369-78.

8. Poiger, H., and C. Schalatter. 1986. Pharmacokinetics of 2,3,7,8-TCDD in man. *Chemosphere* 15:1489-94.

9. Jackson, W.G., Jr., and J.E. Michalek. 2001. Temporal changes in TCDD levels in 1,419 Air Force Vietnam-era veterans not occupationally exposed to herbicides. *Journal of Toxicology and Environmental Health* 11:50-5.

10. Kissel, J.C., and G.M. Robarge. 1988. Assessing the elimination of 2,3,7,8-TCDD from humans with a physiologically based pharmacokinetic model. *Chemosphere* 17:2017-27.

11. Akins, J. R., K. Waldrep, and J.T. Bernert, Jr. 1989. The estimation of total serum lipids by a completely enzymatic "summation" method. *Clinica Chimica Acta* 184:219-26.

12. Patterson, D.G., L. Hampton, C.R. Lapeza, W.T. Belser, V. Green, L. Alexander, and L. Needham. 1987. High resolution gas chromatographic/high-resolution mass spectrometric analysis of human-serum on a whole-weight and lipid basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

13. Patterson, D.G., L.L. Needham, J.L. Pirkle, D.W. Roberts, J.Bagby, W.A. Garret, J.S. Andrews, Jr., H. Falk, J.T. Bernert, E.J. Sampson, and V.N. Houk. 1988. Correlation between serum and adipose tissue levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in 50 persons from Missouri. *Archives of Environmental Toxicology* 17:139-43.

14. Garrow, J.S., and Webster, J. 1985. Quetelet's index (W/H^2) as a measure of fatness. *International Journal of Obesity* 9:147-53.

15. Michalek, J.E., J.L. Pirkle, L.L. Needham, D.G. Patterson, Jr., S.P. Caudill, R.C. Tripathi, and P. Mocarelli. 2002. Pharmacokinetics of 2,3,7,8-tetrachlorodibenzo-p-dioxin in Seveso adults and veterans of Operation Ranch Hand. *Journal of Exposure Analysis and Environmental Epidemiology* 12(1):44-53.

16. Edmond, C., J.E. Michalek, L.S. Birnbaum, and M.J. DeVito. 2004. Use of a PBPK model with dose-dependent elimination rates predicts higher peak dioxin exposures than previously estimated. *Organohalogen Compounds* 66:2655-9.

17. Hornung, R.W., and D.R. Reed. 1990. Estimation of average concentration in the presence of nondetectable values. Applied *Occupational and Environmental Hygiene* 5(1):46-51.

18. SAS Institute, Inc. SAS Language Reference: Version 8. 1999. Cary, NC.

19. Cox, D.R. 1972. Regression models and life tables. *Journal of the Royal Statistical Society, B* 34:187-220.

20. Bishop, Y.M.M., S.E. Feinberg, and P.W. Holland. 1975. *Discrete multivariate analysis: Theory and practice.* MIT Press: Cambridge, MA.

21. Neter, J., and W. Wasserman. 1974. *Applied Linear Statistical Models.* Richard D. Irwin, Inc.: Homewood, IL.

22. Hosmer, D., and S. Lemeshow. 1989. *Applied Logistic Regression.* John Wiley & Sons: New York, NY.

23. Agresti, A. 1990. *Categorical Data Analysis.* John Wiley & Sons: New York, NY.

24. Cox, D.R. 1975. Partial likelihood. *Biometrika* 62:269-76.

25. Kaplan, E.L., and P.L. Meier. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association* 53:457-81.

26. Steel, R.G.D., and J.H. Torrie. 1960. *Principles and Procedures of Statistics.* McGraw-Hill Book Company, Inc.: New York, NY.

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8   COVARIATE ASSOCIATIONS WITH ESTIMATES OF DIOXIN EXPOSURE

8.1   INTRODUCTION

The associations between the covariates used throughout this report and four estimates of dioxin exposure are evaluated in this chapter. The purpose of studying these associations was to determine if these covariates, which have been determined to be associated with one or more of the health endpoints considered in this study, were associated with an estimate of dioxin exposure, and, therefore, could potentially be confounding variables in subsequent statistical analyses in this report. These covariates and estimates of dioxin exposure are used extensively in the statistical analyses in Chapters 9 through 20. Specific definitions of the covariates are contained in those chapters. The results contained in this chapter are associations and should not be interpreted as indicating causal relations between the estimates of dioxin exposure and covariate levels.

Some of the relations between covariates and estimates of dioxin exposure may have been confounded with military occupation. In this report, the unadjusted relations between dioxin exposure and all covariates were evaluated, as were the relations when military occupation was considered.

Four models were examined for each covariate. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. Model 1 examined the relation between the covariate and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the Centers for Disease Control and Prevention (CDC) using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in parts per trillion (ppt) on a lipid weight basis (1). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the covariate and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2.

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. These four categories— Comparisons, background Ranch Hands, low Ranch Hands, and high Ranch Hands—were used in Model 3 analyses. The relation between the covariate in each of the three Ranch Hand categories and the covariate in the

Comparison category was examined. Ranch Hands with no dioxin measurements were excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the covariate and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The summary statistics listed in the tables in this chapter are percentages, correlation coefficients (r), or means. For Models 1 and 3, if a covariate is discrete, the percentage of Ranch Hands and Comparisons is shown for each of the covariate categories and the equality of percentages in each covariate category is tested. If a covariate is continuous, the mean of the covariate is given separately for Ranch Hands and Comparisons and the equality of means is tested.

Because the measure of dioxin is continuous for the analyses of Models 2 and 4, if a covariate is also continuous, a correlation coefficient between initial or 1987 dioxin and the covariate is provided and a test is performed to see if the correlation coefficient is significantly different from zero. If a covariate is discrete, dioxin means for each of the covariate categories are displayed and the equality of dioxin means among each covariate category is tested.

Consistent with the methodology used in each of the clinical chapters, the means presented in the tables were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and for 1987 dioxin in Model 4. For each of the sections below, a written description of the findings is given. A table displaying all the statistics and p-values is given at the end of the section.

8.2   MATCHING DEMOGRAPHIC VARIABLES (AGE, RACE, AND MILITARY OCCUPATION)

Age, race, and military occupation were used in the design of the Air Force Health Study to match Ranch Hand participants with Comparisons to reduce the association between these variables and group status (Model 1). It was impossible, however, to eliminate the possible confounding associations between these variables and serum dioxin in Models 2 through 4 through study design, because the matched design accounted for the possible confounding associations between age, race, and military occupation and group, but not dioxin. Results of tests of association between age, race, and military occupation and the four estimates of dioxin exposure are given in Table 8-1.

Examining the association between age in its continuous form and dioxin revealed significant relations in the unadjusted analyses of Models 2, 3, and 4 ($p<0.001$ for each model). After adjusting for military occupation, however, the association was not significant in Models 2 or 4 ($p=0.333$ and $p=0.645$, respectively) but was significant in Model 3 ($p=0.023$). The highest mean age (64.5 years) was observed in the low Ranch Hand dioxin category and the youngest average age was observed for Ranch Hands in the high dioxin category, with a mean age of 60.1 years. No significant association was seen between group and age in unadjusted and adjusted Model 1 analyses ($p \geq 0.72$ for each analysis).

Dichotomized age (i.e., born before 1942, born in or after 1942) and dioxin exposure showed relations similar to age in its continuous form. Models 2, 3, and 4 were significant in the unadjusted analyses ($p<0.001$ for each analysis). When the relation was adjusted for military occupation, however, the results were no longer significant in Models 2 and 4 ($p=0.080$ and $p=0.712$, respectively), but were significant in Model 3 ($p=0.014$). More Ranch Hands in the low dioxin category (64.9%) were in the older age

category than Ranch Hands in the background category (61.4%), Comparisons (54.1%), or Ranch Hands in the high dioxin category (33.8%). In unadjusted and adjusted Model 1 analyses, no significant difference in age was seen between Ranch Hands and Comparisons (p>0.78) due to the matched study design.

The association between race and dioxin was significant only for Model 2 in the unadjusted analyses (p=0.032). After adjusting for military occupation, however, Models 2, 3, and 4 showed significant results (p<0.001, p=0.013, and p=0.009, respectively). Blacks had lower mean initial and 1987 dioxin levels than did non-Blacks in Models 2 and 4. The mean initial dioxin level in Blacks was 97.1 ppt compared to 140.5 ppt in non-Blacks. Likewise, the 1987 dioxin level was lower in Blacks (12.5 ppt) than in non-Blacks (13.3 ppt). In Model 3, the percentage of Blacks varied among Comparisons (6.5%) and Ranch Hands in the background dioxin category (5.1%), the low dioxin category (10.0%), and the high dioxin category (4.7%). Because participants were matched according to race, no difference in race was seen between exposure groups in unadjusted and adjusted Model 1 analyses (p>0.92 for each analysis).

A significant association was found between military occupation and dioxin in Models 2, 3, and 4 (p<0.001 for each model). In Models 2 and 4, the mean dioxin levels were lowest among officers, followed by enlisted flyers and enlisted groundcrew. As expected, the percentages of officers, enlisted flyers, and enlisted groundcrew were similar between Ranch Hands and Comparisons in Model 1 (p=0.679), but the percentages varied considerably among the three Ranch Hand dioxin categories in Model 3. In Model 3, 61.7 percent of Ranch Hands in the background dioxin category were officers, but only 39.8 percent of Ranch Hands in the low dioxin category and 2.8 percent of Ranch Hands in the high dioxin category were officers. The mean initial dioxin level was 61.8 ppt among officers compared to 125.1 ppt among enlisted flyers and 189.1 ppt among enlisted groundcrew. Similarly the mean 1987 dioxin level was lowest in officers (7.0 ppt), followed by enlisted flyers (15.3 ppt) and enlisted groundcrew (22.5 ppt).

Table 8-1. Associations Between Matching Demographic Variables (Age, Race, and Military Occupation) and Estimates of Herbicide or Dioxin Exposure

Covariate	Covariate Category	Model 1 Mean or n (%) Ranch Hand	Model 1 Mean or n (%) Comparison	Model 1 p-Value Unadjusted	Model 1 p-Value Adjusted[a]
Age (years)	All	777	1,174		
(continuous)		O = 63.1	O = 63.0	0.720	0.908
(discrete)	Born <1942	426 (54.8)	635 (54.1)	0.784	0.955
	Born ≥1942	351 (45.2)	539 (45.9)		
Race	All	777	1,174		
	Black	49 (6.3)	76 (6.5)	0.958	0.923
	Non-Black	728 (93.7)	1,098 (93.5)		
Military Occupation	All	777	1,174		
	Officer	307 (39.5)	462 (39.4)	0.679	--
	Enlisted Flyer	133 (17.1)	185 (15.8)		
	Enlisted Groundcrew	337 (43.4)	527 (44.9)		

Covariate	Covariate Category	Model 2 Correlation or Mean (n) Initial Dioxin (ppt)	Model 2 p-Value Unadjusted	Model 2 p-Value Adjusted[a]
Age (years)	All	424		
(continuous)		r = -0.276	<0.001**	0.333
(discrete)	Born <1942	O = 102.8 (209)	<0.001**	0.080
	Born ≥1942	O = 180.3 (215)		
Race	All	424		
	Black	O = 97.1 (31)	0.032*	<0.001**
	Non-Black	O = 140.5 (393)		
Military Occupation	All	424		
	Officer	O = 61.8 (90)	<0.001**	--
	Enlisted Flyer	O = 125.1 (89)		
	Enlisted Groundcrew	O = 189.1 (245)		

*: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Covariate	Covariate Category	Model 3					
		Mean or n (%)				p-Value	
		Comparison	Ranch Hand			Unadjusted	Adjusted[a]
			Background	Low	High		
Age (years)	All	1,174	352	211	213		
(continuous)		O = 63.0	O = 64.1	O = 64.5	O = 60.1	<0.001**	0.023*
(discrete)	Born <1942	635 (54.1)	216 (61.4)	137 (64.9)	72 (33.8)	<0.001**	0.014*
	Born ≥1942	539 (45.9)	136 (38.6)	74 (35.1)	141 (66.2)		
Race	All	1,174	352	211	213		
	Black	76 (6.5)	18 (5.1)	21 (10.0)	10 (4.7)	0.092	0.013*
	Non-Black	1,098 (93.5)	334 (94.9)	190 (90.0)	203 (95.3)		
Military Occupation	All	1,174	352	211	213		
	Officer	462 (39.4)	217 (61.7)	84 (39.8)	6 (2.8)	<0.001**	--
	Enlisted Flyer	185 (15.8)	43 (12.2)	47 (22.3)	42 (19.7)		
	Enlisted Groundcrew	527 (44.9)	92 (26.1)	80 (37.9)	165 (77.5)		

*: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Covariate	Covariate Category	Model 4		
		Correlation or Mean (n) 1987 Dioxin (ppt)	p-Value	
			Unadjusted	Adjusted[a]
Age (years) (continuous)	All	776 r = -0.195	<0.001**	0.645
(discrete)	Born <1942	O = 10.7 (425)	<0.001**	0.712
	Born ≥1942	O = 17.1 (351)		
Race	All	776		
	Black	O = 12.5 (49)	0.703	0.009**
	Non-Black	O = 13.3 (727)		
Military Occupation	All	776		
	Officer	O = 7.0 (307)	<0.001**	--
	Enlisted Flyer	O = 15.3 (132)		
	Enlisted Groundcrew	O = 22.5 (337)		

[a]Analyses are adjusted for military occupation.

**: Statistically significant (p-value≤0.010).

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and for 1987 dioxin in Model 4.

8.3   ALCOHOL USE

Results of tests of association between alcohol use and the estimates of dioxin exposure are shown in Table 8-2. No significant association was found between dioxin and current alcohol use in unadjusted or adjusted Model 1, 2, or 3 analyses using the continuous form of alcohol use (p>0.10 for each analysis). Model 4 analysis showed a significant unadjusted association between current alcohol use and 1987 dioxin (p=0.016), but this association was not significant when adjusted for military occupation (p=0.254).

The relation between the dichotomized form of current alcohol use and dioxin exposure mirrored the relation between the continuous form of current alcohol use and dioxin exposure. No significant relations were seen between the discrete form of current alcohol use and dioxin in the unadjusted or adjusted analyses of Models 1 through Model 3 (p>0.09 for all analyses). The unadjusted analysis of Model 4 was significant (p=0.041), but the relation was no longer significant after adjustment for military occupation (p=0.294).

The adjusted and unadjusted associations between lifetime alcohol history in its continuous form and dioxin exposure were not significant in Models 1, 3, and 4 (p>0.29 for all analyses). Model 2 showed a significant positive correlation (r=0.106) between lifetime alcohol history and initial dioxin in the unadjusted and adjusted analyses (p=0.030 unadjusted, p=0.009 adjusted).

Similar results were seen in the analysis of the discrete form of lifetime alcohol use. Model 2 unadjusted and adjusted analyses showed a significant relation between lifetime alcohol use and initial dioxin (p=0.030 unadjusted, p=0.019 adjusted). The mean initial dioxin level was higher for nondrinkers (207.6 ppt) than for drinkers with less than 40 drink-years (129.1 ppt) or drinkers with a lifetime alcohol history of more than 40 drink-years (139.4 ppt). No significant associations between lifetime alcohol use and initial dioxin were observed in the unadjusted and adjusted analyses of Models 1, 3, and 4 (p>0.08 for all analyses).

Statistically significant associations were found in the unadjusted analysis of dioxin and current wine use in its continuous form for Model 3 (p=0.009) and Model 4 (p<0.001). Neither of these associations, however, was significant when the models were adjusted for military occupation (p>0.67 for all analyses). No significant associations were seen between current wine use in its continuous form and dioxin in Model 1 or Model 2 for the unadjusted and adjusted models (p>0.05 for all analyses).

Current wine use in its discrete form showed significant association with dioxin exposure in the unadjusted analyses of Model 2 (p=0.001), Model 3 (p<0.001), and Model 4 (p<0.001). None of these associations was significant when military occupation was taken into consideration (p>0.09 for all analyses). No difference in current wine use was observed between Ranch Hands and Comparisons in the unadjusted and adjusted analyses for Model 1 (p>0.31 for both analyses).

Lifetime wine history, in its continuous form, showed significant relations with dioxin in the unadjusted analyses of Model 2, Model 3, and Model 4 (p=0.002, p<0.001, p<0.001, respectively). None of these results was significant when adjusted for military occupation (p>0.15 for all analyses). Unadjusted and adjusted analyses of Model 1 revealed no significant difference in lifetime wine use between Ranch Hands and Comparisons (p>0.31 for each analysis).

The discrete form of lifetime wine use showed significant association with dioxin in the unadjusted analyses of Models 2, 3, and 4 (p<0.001, p=0.014, and p=0.002, respectively). After adjusting for military occupation, the relations were significant for Model 1 and Model 3 (p=0.049 and p=0.047,

respectively) but not significant for Models 2 and 4 (p>0.11 for each analysis). Of all Ranch Hands, 71.5 percent were wine drinkers, as compared to 75.3 percent of Comparisons who were wine drinkers. A higher percentage of Comparisons (75.3%) were wine drinkers than Ranch Hands in the background (75.0%), low (72.9%), and high (64.8%) dioxin categories.

Table 8-2. Associations Between Alcohol Use and Estimates of Herbicide or Dioxin Exposure

| | | Model 1 | | | |
| | | Mean or n (%) | | p-Value | |
Covariate	Covariate Category	Ranch Hand	Comparison	Unadjusted	Adjusted[a]
Current Alcohol Use (drinks/day)	All	777	1,172		
(continuous)		O = 0.51	O = 0.51	0.987	0.993
(discrete)	0-1	655 (84.3)	1,002 (85.5)	0.509	0.459
	>1	122 (15.7)	170 (14.5)		
Lifetime Alcohol History (drink-years)	All	773	1,169		
(continuous)		O = 38.0	O = 39.1	0.669	0.650
(discrete)	0	48 (6.2)	59 (5.1)	0.469	0.451
	>0-40	493 (63.8)	741 (63.4)		
	>40	232 (30.0)	369 (31.6)		
Current Wine Use (drinks/day)	All	777	1,172		
(continuous)		O = 0.13	O = 0.13	0.798	0.782
(discrete)	0	515 (66.3)	754 (64.3)	0.404	0.319
	>0	262 (33.7)	418 (35.7)		
Lifetime Wine History (wine-years)	All	776	1,170		
(continuous)		O = 4.56	O = 4.05	0.325	0.311
(discrete)	0	221 (28.5)	289 (24.7)	0.071	0.049*
	>0	555 (71.5)	881 (75.3)		

*: Statistically significant (0.010<p-value≤0.050).

| | | Model 2 | | | |
| | | Correlation or Mean (n) | p-Value | | |
Covariate	Covariate Category	Initial Dioxin (ppt)	Unadjusted	Adjusted[a]
Current Alcohol Use (drinks/day)	All	424		
(continuous)		r = -0.079	0.102	0.456
(discrete)	0-1	O = 141.2 (360)	0.092	0.468
	>1	O = 114.3 (64)		
Lifetime Alcohol History (drink-years)	All	421		
(continuous)		r = 0.106	0.030*	0.009**
(discrete)	0	O = 207.6 (29)	0.030*	0.019*
	>0-40	O = 129.1 (265)		
	>40	O = 139.4 (127)		

Covariate	Covariate Category	Model 2 Correlation or Mean (n) Initial Dioxin (ppt)	p-Value Unadjusted	p-Value Adjusted[a]
Current Wine Use (drinks/day) (continuous)	All	424 r = -0.092		
(discrete)	0	O = 149.9 (304)	0.058	0.752
	>0	O = 108.3 (120)	0.001**	0.992
Lifetime Wine History (wine-years) (continuous)	All	423 r = -0.151	0.002**	0.152
(discrete)	0	O = 174.8 (132)	<0.001**	0.113
	>0	O = 122.5 (291)		

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).
**: Statistically significant ($p\text{-value} \leq 0.010$).

Covariate	Covariate Category	Model 3 Mean or n (%) Comparison	Ranch Hand Background	Ranch Hand Low	Ranch Hand High	p-Value Unadjusted	p-Value Adjusted[a]
Current Alcohol Use (drinks/day)	All	1,172	352	211	213		
(continuous)		O = 0.51	O = 0.55	O = 0.51	O = 0.45	0.770	0.953
(discrete)	0-1	1,002 (85.5)	294 (83.5)	176 (83.4)	184 (86.4)	0.667	0.767
	>1	170 (14.5)	58 (16.5)	35 (16.6)	29 (13.6)		
Lifetime Alcohol History (drink-years)	All	1,169	351	210	211		
(continuous)		O = 39.1	O = 37.7	O = 34.9	O = 41.5	0.641	0.699
(discrete)	0	59 (5.1)	19 (5.4)	10 (4.8)	19 (9.0)	0.385	0.574
	>0-40	741 (63.4)	227 (64.7)	138 (65.7)	127 (60.2)		
	>40	369 (31.6)	105 (29.9)	62 (29.5)	65 (30.8)		
Current Wine Use (drinks/day)	All	1,172	352	211	213		
(continuous)		O = 0.13	O = 0.17	O = 0.12	O = 0.06	0.009**	0.959
(discrete)	0	754 (64.3)	210 (59.7)	136 (64.5)	168 (78.9)	<0.001**	0.637
	>0	418 (35.7)	142 (40.3)	75 (35.6)	45 (21.1)		
Lifetime Wine History (wine-years)	All	1,170	352	210	213		
(continuous)		O = 4.05	O = 5.87	O = 4.92	O = 2.06	<0.001**	0.497
(discrete)	0	289 (24.7)	88 (25.0)	57 (27.1)	75 (35.2)	0.014*	0.047*
	>0	881 (75.3)	264 (75.0)	153 (72.9)	138 (64.8)		

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).
**: Statistically significant ($p\text{-value} \leq 0.010$).

Covariate	Covariate Category	Model 4		
		Correlation or Mean (n) 1987 Dioxin (ppt)	p-Value	
			Unadjusted	Adjusted[a]
Current Alcohol Use (drinks/day) (continuous)	All	776 r = -0.087	0.016*	0.254
(discrete)	0-1	O = 13.7 (654)	0.041*	0.294
	>1	O = 11.0 (122)		
Lifetime Alcohol History (drink-years) (continuous)	All	772 r = 0.038	0.295	0.385
(discrete)	0	O = 18.6 (48)	0.086	0.370
	>0-40	O = 12.8 (492)		
	>40	O = 13.1 (232)		
Current Wine Use (drinks/day) (continuous)	All	776 r = -0.130	<0.001**	0.675
(discrete)	0	O = 14.8 (514)	<0.001**	0.093
	>0	O = 10.7 (262)		
Lifetime Wine History (wine-years) (continuous)	All	775 r = -0.125	<0.001**	0.686
(discrete)	0	O = 16.1 (220)	0.002**	0.202
	>0	O = 12.2 (555)		

[a]Analyses are adjusted for military occupation.

  *: Statistically significant (0.010<p-value≤0.050).
 **: Statistically significant (p-value≤0.010).

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and for 1987 dioxin in Model 4.

8.4   CIGARETTE SMOKING

Results of tests of association between cigarette smoking and the estimates of dioxin exposure are given in Table 8-3. The mean number of cigarettes smoked per day was significantly higher in Ranch Hands than Comparisons in the unadjusted and adjusted analyses of Model 1 (p=0.011 unadjusted, p=0.010 adjusted). Ranch Hands smoked an average of 3.22 cigarettes per day and Comparisons smoked an average of 2.30 cigarettes per day. No significant associations between the current cigarette smoking in its continuous form and initial dioxin were observed in Model 2 analyses (p>0.17 for both analyses). In Model 3, a significant difference was noted for current cigarette smoking in its continuous form among the dioxin categories in the unadjusted and adjusted analyses (p=0.033 unadjusted, p=0.024 adjusted). The mean number of cigarettes smoked per day was 3.92 for Ranch Hands in the high dioxin category followed by Ranch Hands in the background and low dioxin categories (2.91 cigarettes per day for each) and Comparisons (2.30 cigarettes per day). While the unadjusted analysis of Model 4 showed no

significant association (p=0.376), the adjusted analyses showed current cigarette smoking increasing with increasing 1987 dioxin levels (p=0.030).

Using the discrete form of current cigarette smoking, the results were not significant in the unadjusted analyses of Model 1 through Model 4 (p>0.06 for each analysis). After considering military occupation, significant associations were revealed in Model 3 (p=0.019) and Model 4 (p<0.001), but not in Model 1 or Model 2 (p>0.05 for each analysis). The distribution of smokers was relatively similar among Comparisons, Ranch Hands in the background category, and Ranch Hands in the low dioxin category. Ranch Hands in the high dioxin category had more nonsmokers (32.4%) and fewer former smokers (47.0%), but more participants smoking up to 20 cigarettes per day (16.9%), than Comparisons or Ranch Hands in the other dioxin categories.

No significant associations were observed between lifetime cigarette smoking in its continuous form and dioxin exposure in Model 1, Model 2, and Model 3 for unadjusted or adjusted analyses (p>0.36 for all analyses). In the Model 4 unadjusted analysis, no significant relation was seen between 1987 dioxin levels and lifetime cigarette smoking (p=0.629). After adjusting Model 4 for military occupation, 1987 dioxin levels decreased with increasing lifetime cigarette smoking (p=0.019).

No significant associations between the cigarette smoking in its discrete form and dioxin were observed in Model 1 or Model 3 unadjusted and adjusted analyses (p>0.07 for all analyses). The unadjusted analyses of Model 2 and Model 4 revealed no significant associations between lifetime cigarette smoking and dioxin exposure (p>0.23 for each analysis). After adjusting for military occupation, however, the results of both analyses were significant (p=0.046 for Model 2; p<0.001 for Model 4). The mean initial and 1987 dioxin levels decreased with increasing lifetime cigarette smoking. The mean initial dioxin was 125.9 ppt in heavy smokers (greater than 10 pack-years), 142.4 ppt in moderate smokers (up to 10 pack-years), and 149.4 ppt in nonsmokers. Mean 1987 dioxin levels were 12.7 ppt in heavy smokers, 12.9 ppt in moderate smokers, and 14.3 ppt in nonsmokers.

Table 8-3. Associations Between Cigarette Smoking and Estimates of Herbicide or Dioxin Exposure

| | | Model 1 | | | |
| | | Mean or n (%) | | p-Value | |
Covariate	Covariate Category	Ranch Hand	Comparison	Unadjusted	Adjusted[a]
Current Cigarette Smoking (cigarettes/day)	All	777	1,172		
(continuous)		O = 3.22	O = 2.30	0.011*	0.010**
(discrete)	Never	237 (30.5)	364 (31.1)	0.063	0.052
	Former	412 (53.0)	664 (56.7)		
	0-20	99 (12.7)	115 (9.8)		
	>20	29 (3.7)	29 (2.5)		
Lifetime Cigarette Smoking (pack-years)	All	777	1,171		
(continuous)		O = 16.3	O = 16.1	0.860	0.917
(discrete)	0	237 (30.5)	364 (31.1)	0.934	0.933
	>0-10	199 (25.6)	292 (24.9)		
	>10	341 (43.9)	515 (44.0)		

Table 8-3. Associations Between Cigarette Smoking and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 2		
		Correlation or Mean (n)	p-Value	
Covariate	Covariate Category	Initial Dioxin (ppt)	Unadjusted	Adjusted[a]
Current Cigarette Smoking (cigarettes/day) (continuous)	All	424 r = 0.067	0.171	0.937
(discrete)	Never	O = 149.4 (131)	0.154	0.131
	Former	O = 124.1 (216)		
	0-20	O = 159.3 (60)		
	>20	O = 138.9 (17)		
Lifetime Cigarette Smoking (pack-years) (continuous)	All	424 r = -0.038	0.432	0.406
(discrete)	0	O = 149.4 (131)	0.231	0.046*
	>0-10	O = 142.4 (102)		
	>10	O = 125.9 (191)		

*: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

		Model 3					
		Mean or n (%)				p-Value	
			Ranch Hand				
Covariate	Covariate Category	Comparison	Background	Low	High	Unadjusted	Adjusted[a]
Current Cigarette Smoking (cigarettes/day) All	All	1,172	352	211	213		
(continuous)		O = 2.30	O = 2.91	O = 2.91	O = 3.92	0.033*	0.024*
(discrete)	Never	364 (31.1)	106 (30.1)	62 (29.4)	69 (32.4)	0.108	0.019*
	Former	664 (56.7)	196 (55.7)	116 (55.0)	100 (47.0)		
	0-20	115 (9.8)	39 (11.1)	24 (11.4)	36 (16.9)		
	>20	29 (2.5)	11 (3.1)	9 (4.3)	8 (3.8)		
Lifetime Cigarette Smoking (pack-years)	All	1,171	352	211	213		
(continuous)		O = 16.1	O = 15.7	O = 17.6	O = 15.7	0.759	0.367
(discrete)	0	364 (31.1)	106 (30.1)	62 (29.4)	69 (32.4)	0.834	0.074
	>0-10	292 (24.9)	97 (27.6)	48 (22.8)	54 (25.4)		
	>10	515 (44.0)	149 (42.3)	101 (47.9)	90 (42.3)		

*: Statistically significant (0.010<p-value≤0.050).

| | | Model 4 | | |
| | | Correlation or Mean (n) | p-Value | |
Covariate	Covariate Category	1987 Dioxin (ppt)	Unadjusted	Adjusted[a]
Current Cigarette Smoking (cigarettes/day) (continuous)	All	776 r = 0.032	0.376	0.030*
(discrete)	Never	O = 14.3 (237)	0.282	<0.001**
	Former	O = 12.3 (412)		
	0-20	O = 14.1 (99)		
	>20	O = 15.9 (28)		
Lifetime Cigarette Smoking (pack-years) (continuous)	All	776 r = -0.017	0.629	0.019*
(discrete)	0	O = 14.3 (237)	0.456	<0.001**
	>0-10	O = 12.9 (199)		
	>10	O = 12.7 (340)		

[a]Analyses are adjusted for military occupation.

  *: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).
**: Statistically significant ($p\text{-value} \leq 0.010$).

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and for 1987 dioxin in Model 4.

8.5   EXPOSURE TO CARCINOGENS

Results of tests of association between reported exposure to ionizing radiation, industrial chemicals, herbicides, insecticides, and degreasing chemicals and the estimates of dioxin exposure are presented in Table 8-4. These variables were constructed based on responses given by participants and were intended to indicate only post-Southeast Asia (SEA) exposures to these suspected carcinogens.

The association between reported degreasing chemical exposure and dioxin was significant in the unadjusted analyses of Models 2, 3, and 4 (p<0.001 for each model), but not significant in Model 1 (p=0.098). After adjusting for military occupation, however, the association between reported degreasing chemical exposure and dioxin exposure was not significant in any of the models (p>0.05 for all analyses).

Significant associations between group or dioxin levels and reported exposure to herbicides were observed in Models 1, 3, and 4 unadjusted and adjusted analyses (p<0.001 for each analysis). In Model 1, more than twice as many Ranch Hands (97.4%) than Comparisons (44.6%) reported herbicide exposure. Model 3 results showed a similar relation between Ranch Hands and Comparisons, where more than 95 percent of the Ranch Hands in each category reported herbicide exposure. In Model 4, Ranch Hands who reported exposure to herbicides had a mean 1987 dioxin level of 13.5 ppt, as compared to a mean 1987 dioxin level of 5.8 ppt for Ranch Hands not reporting herbicide exposure. In Model 2, unadjusted and

adjusted analyses showed no significant association between reported herbicide exposure and initial dioxin levels (p>0.47 for both analyses).

The association between industrial chemical exposure and dioxin exposure was significant in the analysis of Models 2, 3, and 4 (p=0.045 for Model 2 and p<0.001 for Models 3 and 4). After adjusting for military occupation, however, these associations were no longer significant (p>0.44 for all analyses). No significant difference in industrial chemical exposure was seen between Ranch Hands and Comparisons in Model 1 unadjusted and adjusted analyses (p>0.68 for all analyses).

Significant associations were observed between insecticide exposure and group in Model 1 unadjusted and adjusted analyses (p<0.001), as well as between insecticide exposure and categorized dioxin in Model 3 unadjusted and adjusted analyses (p<0.001). In Model 1, 81.7 percent of Ranch Hands reported exposure to insecticides, in contrast to 66.9 percent of Comparisons. In Model 3, the percentage of participants exposed to insecticides was similar among the Ranch Hand dioxin categories (81.8% for Ranch Hands in the background dioxin category, 81.5% for Ranch Hands in the low dioxin category, and 81.7 % for Ranch Hands in the high dioxin category) and lower for Comparisons (66.9%). No significant relation was seen between insecticide exposure and dioxin in Model 2 or Model 4 unadjusted and adjusted analyses (p>0.12 for all analyses).

A significant difference between the percentage of participants who have been exposed to ionizing radiation was seen between Ranch Hands (22.3%) and Comparisons (26.7%) in Model 1 unadjusted and adjusted analyses (p=0.032 unadjusted, p=0.024 adjusted). No significant associations were seen between dioxin exposure estimates and ionizing radiation exposure in Models 2 through 4 unadjusted and adjusted analyses (p>0.05 for all analyses).

Table 8-4. Associations Between Exposure to Carcinogens and Estimates of Herbicide or Dioxin Exposure

		Model 1			
		n (%)		p-Value	
Covariate	Covariate Category	Ranch Hand	Comparison	Unadjusted	Adjusted[a]
Degreasing Chemical Exposure	All	777	1,174		
	Yes	519 (66.8)	740 (63.0)	0.098	0.058
	No	258 (33.2)	434 (37.0)		
Herbicide Exposure	All	777	1,174		
	Yes	757 (97.4)	523 (44.6)	<0.001**	<0.001**
	No	20 (2.6)	651 (55.4)		
Industrial Chemical Exposure	All	777	1,174		
	Yes	488 (62.8)	729 (62.1)	0.788	0.685
	No	289 (37.2)	445 (37.9)		
Insecticide Exposure	All	777	1,174		
	Yes	635 (81.7)	785 (66.9)	<0.001**	<0.001**
	No	142 (18.3)	389 (33.1)		

		Model 1			
		n (%)		p-Value	
Covariate	Covariate Category	Ranch Hand	Comparison	Unadjusted	Adjusted[a]
Ionizing Radiation Exposure	All	777	1,174		
	Yes	173 (22.3)	313 (26.7)	0.032*	0.024*
	No	604 (77.7)	861 (73.3)		

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

		Model 2		
	Covariate Category	Mean (n) Initial Dioxin (ppt)	p-Value	
Covariate			Unadjusted	Adjusted[a]
Degreasing Chemical Exposure	All	424		
	Yes	O = 150.2 (320)	<0.001**	0.730
	No	O = 102.3 (104)		
Herbicide Exposure	All	424		
	Yes	O = 136.3 (420)	0.475	0.481
	No	O = 190.0 (4)		
Industrial Chemical Exposure	All	424		
	Yes	O = 145.1 (296)	0.045*	0.444
	No	O = 119.3 (128)		
Insecticide Exposure	All	424		
	Yes	O = 134.8 (346)	0.508	0.122
	No	O = 145.6 (78)		
Ionizing Radiation Exposure	All	424		
	Yes	O = 123.8 (91)	0.246	0.397
	No	O = 140.5 (333)		

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

		Model 3					
		n (%)					
			Ranch Hand			p-Value	
Covariate	Covariate Category	Comparison	Background	Low	High	Unadjusted	Adjusted[a]
Degreasing Chemical Exposure	All	1,174	352	211	213		
	Yes	740 (63.0)	198 (56.3)	142 (67.3)	178 (83.6)	<0.001**	0.119
	No	434 (37.0)	154 (43.7)	69 (32.7)	35 (16.4)		
Herbicide Exposure	All	1,174	352	211	213		
	Yes	52 (44.6)	336 (95.5)	209 (99.1)	211 (99.1)	<0.001**	<0.001**
	No	651 (55.4)	16 (4.5)	2 (1.0)	2 (0.9)		

Covariate	Covariate Category	Model 3					
		n (%)				p-Value	
		Comparison	Ranch Hand			Unadjusted	Adjusted[a]
			Background	Low	High		
Industrial Chemical Exposure	All	1,174	352	211	213		
	Yes	729 (62.1)	191 (54.3)	138 (65.4)	158 (74.2)	<0.001**	0.678
	No	445 (37.9)	161 (45.7)	73 (34.6)	55 (25.8)		
Insecticide Exposure	All	1,174	352	211	213		
	Yes	785 (66.9)	288 (81.8)	172 (81.5)	174 (81.7)	<0.001**	<0.001**
	No	389 (33.1)	64 (18.2)	39 (18.5)	39 (18.3)		
Ionizing Radiation Exposure	All	1,174	352	211	213		
	Yes	313 (26.7)	81 (23.0)	52 (24.6)	39 (18.3)	0.056	0.081
	No	861 (73.3)	271 (77.0)	159 (75.4)	174 (81.7)		

**: Statistically significant (p-value≤0.010).

Covariate	Covariate Category	Model 4		
		Mean (n) 1987 Dioxin (ppt)	p-Value	
			Unadjusted	Adjusted[a]
Degreasing Chemical Exposure	All	776		
	Yes	O = 16.1 (518)	<0.001**	0.212
	No	O = 8.9 (258)		
Herbicide Exposure	All	776		
	Yes	O = 13.5 (756)	<0.001**	<0.001**
	No	O = 5.8 (20)		
Industrial Chemical Exposure	All	776		
	Yes	O = 15.3 (487)	<0.001**	0.925
	No	O = 10.3 (289)		
Insecticide Exposure	All	776		
	Yes	O = 13.3 (634)	0.905	0.673
	No	O = 13.1 (142)		
Ionizing Radiation Exposure	All	776		
	Yes	O = 11.7 (172)	0.107	0.141
	No	O = 13.7 (604)		

[a]Analyses are adjusted for military occupation.

**: Statistically significant (p-value≤0.010).

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and for 1987 dioxin in Model 4.

8.6   HEALTH VARIABLES

Results of tests of association between numerous measures related to a participant's health and the estimates of dioxin exposure are presented in Table 8-5.

No significant relations between body mass index in its continuous form and dioxin were demonstrated in the unadjusted and adjusted analyses of Model 1 and Model 2 (p>0.15 for all analyses). In Model 3 unadjusted and adjusted analyses, body mass index differed significantly between Comparisons and Ranch Hands categorized by dioxin levels (p<0.001 for all analyses). The mean body mass index was 29.0 kg/m^2 for Comparisons, 27.8 kg/m^2 for Ranch Hands in the background category, 29.9 kg/m^2 for Ranch Hands in the low category, and 30.3 kg/m^2 for Ranch Hands in the high category. Likewise, Model 4 results showed that body mass index was positively correlated with 1987 dioxin levels (r=0.256) in the unadjusted and adjusted analyses (p<0.001 for each analysis).

The discrete form of body mass index showed results similar to those of the continuous form. No association was detected in the unadjusted or adjusted analyses of Model 1 and Model 2 (p>0.51 for all analyses). Model 3 results were significant for both the unadjusted and adjusted analyses (p<0.001 for each analysis). The percent of Ranch Hands who were classified as obese rose with the dioxin level (23.1% of background Ranch Hands were categorized as obese compared to 44.1% of Ranch Hands in the low dioxin category and 47.0% of Ranch Hands in the high dioxin category). In contrast, 35.4 percent of Comparisons were classified as obese. Obese Ranch Hands had significantly higher 1987 dioxin levels (18.0 ppt) in Model 4 unadjusted and adjusted analyses than participants who were not obese (11.2 ppt) (p<0.001 for all analyses).

No association was seen between dioxin and cholesterol levels in the discrete or continuous form, either with or without adjustment for military occupation in Model 1 through Model 4 (p>0.07 for all analyses).

High-density lipoprotein (HDL) cholesterol in its continuous form showed significant associations with dioxin in Model 2 (p=0.003), Model 3 (p<0.001), and Model 4 (p<0.001). When adjusted for military occupation, the association became nonsignificant in Model 2 (p=0.094). The adjusted association remained significant in Model 3 (p=0.044) and Model 4 (r=-0.180; p=0.003), with HDL levels decreasing as the mean dioxin levels increased. In Model 3, the mean HDL level was 46.1 mg/dL for Comparisons, 48.2 mg/dL for background Ranch Hands, 46.0 mg/dL for Ranch Hands in the low dioxin category, and 42.6 mg/dL for Ranch Hands in the high dioxin category.

In the analysis of the discrete form of HDL, no significant results were seen in the unadjusted or adjusted analyses of Model 2 or Model 4 (p>0.06 for all analyses). In Model 1, no significant associations between HDL and dioxin were noted in the unadjusted analyses (p=0.058), but the results were significant after adjusting for military occupation (p=0.049). HDL values greater than 35 mg/dL were seen in 78.6 percent of Ranch Hands versus 82.2 percent of Comparisons. A significant association was seen between HDL in its discrete form and dioxin in the unadjusted analysis of Model 3 (p=0.020). The association was not significant after adjusting for military occupation (p=0.153).

Statistically significant unadjusted associations were found between the cholesterol-HDL ratio in its continuous form and dioxin for Model 2 (p=0.011), Model 3 (p<0.001), and Model 4 (p<0.001). These associations were not significant when adjusted for military occupation (p>0.11 for all analyses). Neither the unadjusted nor the adjusted Model 1 analyses were significant (p>0.80 for both analyses).

Dichotomizing the cholesterol-HDL ratio using a cutpoint of 5.0 revealed significant associations with dioxin for Models 3 and 4 (p=0.008 for Model 3; p<0.001 for Model 4). The associations between the categorized cholesterol-HDL ratio and dioxin levels were no longer significant after adjusting for military occupation (p>0.26 for both analyses). Unadjusted and adjusted analyses of Model 1 and Model 2 showed no significant findings (p≥0.13 for all analyses).

The examination of the physical activity index showed a significant association with dioxin in the unadjusted Model 1 through Model 4 analyses (p=0.037 for Model 1; p<0.001 for Model 2; p=0.005 for Model 3; p<0.001 for Model 4). More Comparisons were classified as sedentary (51.6%) than Ranch Hands (46.6%). The percent of sedentary Ranch Hands increased as the dioxin levels increased in the dioxin categories of Model 3. In the background dioxin category, 41.2% of Ranch Hands were sedentary versus 46.0% of Ranch Hands in the low dioxin category and 56.3% of Ranch Hands in the high dioxin category. In Model 2, the mean initial dioxin level was lower in moderately active participants (111.2 ppt) and very active participants (111.4 ppt) than sedentary participants (166.4 ppt). Model 4 results were similar to Model 2, with mean 1987 dioxin levels being lowest in the moderately active category (11.3 ppt), followed by very active participants (11.5 ppt) and sedentary participants (15.6 ppt). With the exception of Model 3, these associations remained significant after adjusting for military occupation (p=0.038 for Model 1; p<0.001 for Model 2; p=0.078 for Model 3; p=0.011 for Model 4).

A significant association between diabetic class and dioxin was revealed in the unadjusted Model 3 and Model 4 analyses (p=0.003 for Model 3; p<0.001 for Model 4), and the results remained significant after adjusting for military occupation (p=0.009 for Model 3; p<0.001 for Model 4). More participants were classified as diabetic as the dioxin levels increased in Model 3. For Ranch Hands in the background dioxin category, 11.9 percent of participants were classified as diabetic. In the low dioxin category, 22.8 percent of Ranch Hands were classified as diabetic; 24.4 percent of Ranch Hands in the high dioxin category were classified as diabetic. In Model 4, participants classified as diabetic had higher mean 1987 dioxin levels (18.9 ppt) than participants whose diabetic status was classified as impaired (11.8 ppt) or normal (12.4 ppt). Model 2 showed a significant association between diabetic class and initial dioxin levels only after adjusting for military occupation (p=0.285 unadjusted, p=0.048 adjusted). The mean initial dioxin level was 136.1 ppt for normal participants compared to 122.8 ppt for participants with impaired diabetic status and 152.0 ppt for diabetics. No difference in diabetic class was seen between Ranch Hands and Comparisons in Model 1 unadjusted and adjusted analyses (p>0.70 for all analyses).

The analysis of family history of diabetes revealed no significant associations with dioxin levels in Models 1 through Model 4 in the unadjusted or adjusted analyses (p>0.05 for all analyses).

Participants who were not diagnosed as diabetic prior to the 2002 physical examination, but were suspected to be diabetic based on glucose levels, were recommended to seek follow-up tests. Those participants who were subsequently confirmed to be diabetic were assigned a value of 0 years for duration of diabetes. Nondiabetic participants were also assigned a value of 0 years for duration of diabetes. Significant associations were observed between duration of diabetes in its continuous form and dioxin exposures in Model 2, Model 3, and Model 4; the associations remained significant after adjusting for military occupation (p<0.03 for all analyses). The duration of diabetes increased as initial dioxin levels increased in Model 2 (r=0.104) and as 1987 dioxin levels increased in Model 4 (r=0.146). Likewise, the mean duration of diabetes in Ranch Hands increased with increasing dioxin categories in Model 3. Ranch Hands in the high dioxin category had diabetes for an average of 2.48 years compared to Ranch Hands in the low dioxin category (2.14 years), Ranch Hands in the background category (1.05 years), and Comparisons (1.42 years). No significant difference in duration of diabetes was seen between Ranch

Hands and Comparisons in Model 1 unadjusted and adjusted analyses (p=0.141 unadjusted, p=0.145 adjusted).

The dichotomized form of duration of diabetes showed results similar to the continuous form. Model 3 and Model 4 demonstrated significant associations between duration of diabetes and dioxin exposure in the unadjusted and adjusted analyses (p<0.001 for each analysis). The analysis of Model 2 showed significant results in the adjusted analysis (p=0.014), but not the unadjusted analysis (p=0.167). No difference in duration of diabetes was seen between Ranch Hands and Comparisons in Model 1 unadjusted and adjusted analyses (p>0.86 for all analyses). Higher initial and 1987 dioxin levels were seen for participants who were previously diagnosed as diabetic than for nondiabetics or newly diagnosed diabetics (154.2 ppt versus 132.4 ppt for initial dioxin; 20.1 ppt versus 12.2 ppt for 1987 dioxin). Among Ranch Hands, the percentage of participants who were previously diagnosed as diabetic increased with increasing dioxin level categories (9.1%, 19.4%, and 22.5% in the background, low, and high dioxin categories, respectively).

No significant associations were observed between family history of heart disease or family history of heart disease before age 45 and any of the estimates of dioxin exposure in Model 1 through Model 4 unadjusted and adjusted analyses (p>0.20 for all analyses).

Mean uric acid levels differed significantly between Ranch Hands and Comparisons in Model 1 unadjusted and adjusted analyses (p=0.026 for all analyses) and between Comparisons and Ranch Hands in the various dioxin categories in Model 3 (p=0.019 unadjusted, p=0.010 adjusted). The mean uric acid level was 5.85 mg/dL for Comparisons and 5.72 mg/dL for all Ranch Hands. When Ranch Hands were categorized by dioxin levels in Model 3, mean uric acid levels increased with increasing dioxin levels. The mean uric acid level for Ranch Hands in the background category was 5.61 mg/dL compared to 5.79 mg/dL for Ranch Hands in the low dioxin category and 5.85 mg/dL for Ranch Hands in the high dioxin category. No significant differences in mean uric acid levels were seen in Model 2 or Model 4 unadjusted and adjusted analyses (p>0.12 for all analyses).

When uric acid levels were dichotomized, Model 1, Model 2, and Model 4 showed no significant associations between dioxin and uric acid in unadjusted or adjusted analyses (p>0.07 for all analyses). In Model 3, significant differences in the percent of participants with uric acid levels greater than 5.5 mg/dL were seen between Comparisons and Ranch Hands in the various dioxin categories in the unadjusted analysis (p=0.016) and the adjusted analysis (p=0.009). Ranch Hands in the low dioxin category were more likely to have had a high uric acid level (57.8%) than Comparisons (55.7%), Ranch Hands in the high dioxin category (54.0%), or Ranch Hands in the background category (46.6%).

Significant relations were noted between waist-to-hip ratio measurements in the continuous form and dioxin for Model 3 and Model 4 before and after adjustment for military occupation (p<0.001 for all analyses). The mean waist-to-hip ratio varied from 0.99 for Ranch Hands in the background category to 1.00 for Comparisons, 1.01 for Ranch Hands in the low dioxin category, and 1.02 for Ranch Hands in the high dioxin category. In Model 4 analysis, the waist-to-hip ratio was increased with increasing 1987 dioxin levels (r=0.200). Model 2 analysis showed no significant results in the unadjusted analysis (p=0.108), but was significant when adjusted for military occupation (p=0.006). Initial dioxin levels were positively correlated (r=0.078) with waist-to-hip ratios. No difference in waist-to-hip ratios was seen between Ranch Hands and Comparisons in Model 1 unadjusted and adjusted analyses (p>0.80 for each).

Significant relations were also seen between waist-to-hip ratio measurements in the discrete form and dioxin for Model 3 and Model 4 before and after adjustment for military occupation (p<0.001 for all

analyses). The percentage of participants with a waist-to-hip ratio greater than 1.0 increased as dioxin levels increased in Model 3. Ranch Hands in the high dioxin category were more likely to have a waist greater than their hip circumference (59.6%) than Ranch Hands in the low dioxin category (53.1%), Ranch Hands in the background category (37.6%), or Comparisons (49.8%). Mean 1987 dioxin levels were higher in participants with a waist greater than the hip circumference (16.5 ppt) than in participants with a waist-to-hip ratio less than or equal to 1.0 (10.8 ppt). Model 2 analysis also showed significant results in the unadjusted (p=0.018) and adjusted results (p=0.008). The mean initial dioxin was 121.2 ppt for participants with a waist less than or equal to the hip circumference. For those participants with a waist-to-hip ratio greater than 1.0, the mean initial dioxin was 150.1 ppt. No difference in the waist-to-hip ratio was seen between Ranch Hands and Comparisons in Model 1 unadjusted and adjusted analyses (p>0.35 for each analysis).

When examining the relation between current blood pressure medication use and dioxin exposure, no significant relation was observed in Model 1, Model 2, or Model 3, whether or not adjustment was made for military occupation (p>0.06 for all analyses). In Model 4, the unadjusted analysis was significant (p=0.037), as was the adjusted analysis (p=0.025). Mean 1987 dioxin levels were higher in participants currently taking medication for high blood pressure (14.5 ppt) than for those not taking medication (12.3 ppt).

No significant relations between current use of alpha- or beta-adrenergic blocking agents and dioxin exposure were seen in the unadjusted or adjusted analyses of Model 1 through Model 4 (p>0.27 for all analyses).

The relation between current angiotensin-converting enzyme (ACE) inhibitor use and dioxin exposure was not significant in Model 1, Model 2, or Model 3 unadjusted and adjusted analyses (p>0.10 for all analyses). The unadjusted analysis of Model 4 showed a significant association between 1987 dioxin levels and current ACE inhibitor use (p=0.028). After adjusting for military occupation, however, the results were no longer significant (p=0.055).

No significant associations were noted between dioxin exposure and current calcium channel blocker use in any of the unadjusted and adjusted analyses using the four models (p>0.14 for all analyses) or between dioxin exposure and current diuretic use (p>0.12 for all analyses).

Table 8-5. Associations Between Health Variables and Estimates of Herbicide or Dioxin Exposure

| | | Model 1 | | | |
| | | Mean or n (%) | | p-Value | |
Covariate	Covariate Category	Ranch Hand	Comparison	Unadjusted	Adjusted[a]
Body Mass Index (kg/m^2)	All	776	1,174		
(continuous)		O = 29.0	O = 29.0	0.944	0.924
(discrete)	Not Obese (≤30)	502 (64.7)	759 (64.7)	0.999	0.997
	Obese (>30)	274 (35.3)	415 (35.4)		

Covariate	Covariate Category	Model 1			
		Mean or n (%)		p-Value	
		Ranch Hand	Comparison	Unadjusted	Adjusted[a]
Cholesterol (mg/dL)	All	777	1,174		
(continuous)		$\bar{x}$ = 196.2	$\bar{x}$ = 199.2	0.079	0.081
(discrete)	0-200	439 (56.5)	623 (53.1)	0.137	0.139
	>200-239	252 (32.4)	388 (33.1)		
	>239	86 (11.1)	163 (13.9)		
HDL (mg/dL)	All	777	1,174		
(continuous)		$\bar{x}$ = 46.1	$\bar{x}$ = 46.1	0.955	0.931
(discrete)	0-35	166 (21.4)	209 (17.8)	0.058	0.049*
	>35	611 (78.6)	965 (82.2)		
Cholesterol-HDL Ratio	All	777	1,174		
(continuous)		$\bar{x}$ = 4.54	$\bar{x}$ = 4.56	0.802	0.830
(discrete)	0-5	532 (68.5)	795 (67.7)	0.765	0.753
	>5	245 (31.5)	379 (32.3)		
Physical Activity Index	All	777	1,172		
	Sedentary	362 (46.6)	605 (51.6)	0.037*	0.038*
	Moderate	155 (20.0)	236 (20.1)		
	Very Active	260 (33.5)	331 (28.2)		
Diabetic Class[b]	All	777	1,174		
	Normal	467 (60.1)	709 (60.4)	0.707	0.713
	Impaired	168 (21.6)	238 (20.3)		
	Diabetic	142 (18.3)	227 (19.3)		
Family History of Diabetes	All	769	1,165		
	Yes	244 (31.7)	371 (31.9)	0.997	0.968
	No	525 (68.3)	794 (68.2)		
Duration of Diabetes (years)[c]	All	777	1,174		
(continuous)		$\bar{x}$ = 1.74	$\bar{x}$ = 1.42	0.141	0.145
(discrete)	0	656 (84.4)	955 (84.8)	0.896	0.861
	>0	121 (15.6)	179 (15.3)		
Family History of Heart Disease	All	771	1,169		
	Yes	498 (64.6)	739 (63.2)	0.570	0.552
	No	273 (35.4)	430 (36.8)		
Family History of Heart Disease Before Age 45	All	749	1,150		
	Yes	76 (10.2)	118 (10.3)	0.998	0.952
	No	673 (89.9)	1,032 (89.7)		
Uric Acid (mg/dL)	All	777	1,174		
(continuous)		$\bar{x}$ = 5.72	$\bar{x}$ = 5.85	0.026*	0.026*
(discrete)	0-5.5	376 (48.4)	520 (44.3)	0.083	0.074
	>5.5	401 (51.6)	654 (55.7)		

Covariate	Covariate Category	Model 1			
		Mean or n (%)		p-Value	
		Ranch Hand	Comparison	Unadjusted	Adjusted[a]
Waist-to-hip Ratio	All	776	1,173		
(continuous)		O = 1.00	O = 1.00	0.807	0.844
(discrete)	0-1.0	405 (52.2)	589 (50.2)	0.419	0.358
	>1.0	371 (47.8)	584 (49.8)		
Currently Taking Blood Pressure Medication	All	777	1,174		
	Yes	344 (44.3)	521 (44.4)	0.999	0.915
	No	433 (55.7)	653 (55.6)		
Currently Taking Alpha- or Beta-Adrenergic Blocking Agents	All	777	1,174		
	Yes	167 (21.5)	249 (21.2)	0.926	0.920
	No	610 (78.5)	925 (78.8)		
Currently Taking ACE Inhibitors	All	777	1,174		
	Yes	187 (24.1)	302 (25.7)	0.439	0.400
	No	590 (75.9)	872 (74.3)		
Currently Taking Calcium Channel Blockers	All	777	1,174		
	Yes	99 (12.7)	158 (13.5)	0.697	0.623
	No	678 (87.3)	1,016 (86.5)		
Currently Taking Diuretics	All	777	1,174		
	Yes	106 (13.6)	156 (13.3)	0.875	0.828
	No	671 (86.4)	1,018 (86.7)		

*: Statistically significant (0.010<p-value≤0.050).

Covariate	Covariate Category	Model 2		
		Correlation or Mean (n) Initial Dioxin (ppt)	p-Value	
			Unadjusted	Adjusted[a]
Body Mass Index (kg/m^2) (continuous)	All	424 r = 0.064	0.192	0.156
(discrete)	Not Obese (≤30)	O = 134.2 (231)	0.654	0.518
	Obese (>30)	O = 139.8 (193)		
Cholesterol (mg/dL) (continuous)	All	424 r = 0.017	0.728	0.777
(discrete)	0-200	O = 129.5 (244)	0.348	0.544
	>200-239	O = 149.1 (135)		
	>239	O = 141.9 (45)		
HDL (mg/dL) (continuous)	All	424 r = -0.145	0.003**	0.094
(discrete)	0-35	O = 144.6 (101)	0.486	0.572
	>35	O = 134.4 (323)		

Covariate	Covariate Category	Model 2 Correlation or Mean (n) Initial Dioxin (ppt)	p-Value Unadjusted	p-Value Adjusted[a]
Cholesterol-HDL Ratio (continuous)	All	424 r = 0.124	0.011*	0.373
(discrete)	0-5	O = 129.9 (271)	0.130	0.969
	>5	O = 149.7 (153)		
Physical Activity Index	All	424		
	Sedentary	O = 166.4 (217)	<0.001**	<0.001**
	Moderate	O = 111.2 (77)		
	Very Active	O = 111.4 (130)		
Diabetic Class[b]	All	424		
	Normal	O = 136.1 (235)	0.285	0.048*
	Impaired	O = 122.8 (89)		
	Diabetic	O = 152.0 (100)		
Family History of Diabetes	All	418		
	Yes	O = 146.4 (141)	0.303	0.670
	No	O = 132.6 (277)		
Duration of Diabetes (years)[c] (continuous)	All	424 r = 0.104	0.032*	<0.001**
(discrete)	0	O = 132.4 (335)	0.167	0.014*
	>0	O = 154.2 (89)		
Family History of Heart Disease	All	420		
	Yes	O = 134.9 (275)	0.717	0.986
	No	O = 139.5 (145)		
Family History of Heart Disease Before Age 45	All	405		
	Yes	O = 148.1 (41)	0.635	0.999
	No	O = 137.8 (364)		
Uric Acid (mg/dL) (continuous)	All	424 r = -0.013	0.788	0.526
(discrete)	0-5.5	O = 143.3 (187)	0.353	0.820
	>5.5	O = 131.8 (237)		
Waist-to-hip Ratio (continuous)	All	424 r = 0.078	0.108	0.006**
(discrete)	0-1.0	O = 121.2 (185)	0.018*	0.008**
	>1.0	O = 150.1 (239)		
Currently Taking Blood Pressure Medication	All	424		
	Yes	O = 138.4 (203)	0.801	0.378
	No	O = 135.3 (221)		

Covariate	Covariate Category	Model 2 Correlation or Mean (n) Initial Dioxin (ppt)	p-Value Unadjusted	p-Value Adjusted[a]
Currently Taking Alpha- or Beta-Adrenergic Blocking Agents	All	424		
	Yes	$\bar{x}$ = 132.9 (91)	0.738	0.292
	No	$\bar{x}$ = 137.8 (333)		
Currently Taking ACE Inhibitors	All	424		
	Yes	$\bar{x}$ = 151.1 (113)	0.180	0.104
	No	$\bar{x}$ = 131.9 (311)		
Currently Taking Calcium Channel Blockers	All	424		
	Yes	$\bar{x}$ = 120.5 (56)	0.273	0.145
	No	$\bar{x}$ = 139.4 (368)		
Currently Taking Diuretics	All	424		
	Yes	$\bar{x}$ = 134.4 (67)	0.869	0.961
	No	$\bar{x}$ = 137.2 (357)		

*: Statistically significant ($0.010 < p\text{-value} \le 0.050$).
**: Statistically significant ($p\text{-value} \le 0.010$).

Covariate	Covariate Category	Model 3 Mean or n (%) Comparison	Ranch Hand Background	Ranch Hand Low	Ranch Hand High	p-Value Unadjusted	p-Value Adjusted[a]
Body Mass Index (kg/m^2)	All	1,174	351	211	213		
(continuous)		$\bar{x}$ = 29.0	$\bar{x}$ = 27.8	$\bar{x}$ = 29.9	$\bar{x}$ = 30.3	<0.001**	<0.001**
(discrete)	Not Obese ($\le$30)	759 (64.7)	270 (76.9)	118 (55.9)	113 (53.1)	<0.001**	<0.001**
	Obese (>30)	415 (35.4)	81 (23.1)	93 (44.1)	100 (47.0)		
Cholesterol (mg/dL)	All	1,174	352	211	213		
(continuous)		$\bar{x}$ = 199.2	$\bar{x}$ = 196.2	$\bar{x}$ = 195.5	$\bar{x}$ = 196.9	0.368	0.281
(discrete)	0-200	623 (53.1)	194 (55.1)	130 (61.6)	114 (53.5)	0.305	0.225
	>200-239	388 (33.1)	117 (33.2)	61 (28.9)	74 (34.7)		
	>239	163 (13.9)	41 (11.7)	20 (9.5)	25 (11.7)		
HDL (mg/dL)	All	1,174	352	211	213		
(continuous)		$\bar{x}$ = 46.1	$\bar{x}$ = 48.2	$\bar{x}$ = 46.0	$\bar{x}$ = 42.6	<0.001**	0.044*
(discrete)	0-35	209 (17.8)	65 (18.5)	44 (20.9)	57 (26.8)	0.020*	0.153
	>35	965 (82.2)	287 (81.5)	167 (79.2)	156 (73.2)		

		Model 3					
		Mean or n (%)				p-Value	
			Ranch Hand				
Covariate	Covariate Category	Comparison	Background	Low	High	Unadjusted	Adjusted[a]
Cholesterol-HDL Ratio	All	1,174	352	211	213		
(continuous)		O = 4.56	O = 4.36	O = 4.53	O = 4.86	<0.001**	0.413
(discrete)	0-5	795 (67.7)	260 (73.9)	143 (67.8)	128 (60.1)	0.008**	0.573
	>5	379 (32.3)	92 (26.1)	68 (32.2)	85 (39.9)		
Physical Activity Index	All	1,172	352	211	213		
	Sedentary	605 (51.6)	145 (41.2)	97 (46.0)	120 (56.3)	0.005**	0.078
	Moderate	236 (20.1)	78 (22.2)	43 (20.4)	34 (16.0)		
	Very Active	331 (28.2)	129 (36.7)	71 (33.7)	59 (27.7)		
Diabetic Class[b]	All	1,174	352	211	213		
	Normal	709 (60.4)	231 (65.6)	113 (53.6)	122 (57.3)	0.003**	0.009**
	Impaired	238 (20.3)	79 (22.4)	50 (23.7)	39 (18.3)		
	Diabetic	227 (19.3)	42 (11.9)	48 (22.8)	52 (24.4)		
Family History of Diabetes	All	1,165	350	207	211		
	Yes	371 (31.9)	103 (29.4)	66 (31.9)	75 (35.6)	0.518	0.986
	No	794 (68.2)	247 (70.6)	141 (68.1)	136 (64.5)		
Duration of Diabetes (years)[c]	All	1,174	352	211	213		
(continuous)		O = 1.42	O = 1.05	O = 2.14	O = 2.48	0.001**	<0.001**
(discrete)	0	995 (84.8)	320 (90.9)	170 (80.6)	165 (77.5)	<0.001**	<0.001**
	>0	179 (15.3)	32 (9.1)	41 (19.4)	48 (22.5)		
Family History of Heart Disease	All	1,169	350	208	212		
	Yes	739 (63.2)	223 (63.7)	139 (66.8)	136 (64.2)	0.799	0.589
	No	430 (36.8)	127 (36.3)	69 (33.2)	76 (35.9)		
Family History of Heart Disease Before Age 45	All	1,150	343	196	209		
	Yes	118 (10.3)	35 (10.2)	17 (8.7)	24 (11.5)	0.831	0.902
	No	1,032 (89.7)	308 (89.8)	179 (91.3)	185 (88.5)		
Uric Acid (mg/dL)	All	1,174	352	211	213		
(continuous)		O = 5.85	O = 5.61	O = 5.79	O = 5.85	0.019*	0.010**
(discrete)	0-5.5	520 (44.3)	188 (53.4)	89 (42.2)	98 (46.0)	0.016*	0.009**
	>5.5	654 (55.7)	164 (46.6)	122 (57.8)	115 (54.0)		
Waist-to-hip Ratio	All	1,173	351	211	213		
(continuous)		O = 1.00	O = 0.99	O = 1.01	O = 1.02	<0.001**	<0.001**
(discrete)	0-1.0	589 (50.2)	219 (62.4)	99 (46.9)	86 (40.4)	<0.001**	<0.001**
	>1.0	584 (49.8)	132 (37.6)	112 (53.1)	127 (59.6)		

		Model 3					
		Mean or n (%)				p-Value	
				Ranch Hand			
Covariate	Covariate Category	Comparison	Background	Low	High	Unadjusted	Adjusted[a]
Currently Taking Blood Pressure Medication	All	1,174	352	211	213		
	Yes	521 (44.4)	141 (40.1)	98 (46.5)	105 (49.3)	0.164	0.063
	No	653 (55.6)	211 (59.9)	113 (53.6)	108 (50.7)		
Currently Taking Alpha- or Beta-Adrenergic Blocking Agents	All	1,174	352	211	213		
	Yes	249 (21.2)	76 (21.6)	45 (21.3)	46 (21.6)	0.998	0.782
	No	925 (78.8)	276 (78.4)	166 (78.7)	167 (78.4)		
Currently Taking ACE Inhibitors	All	1,174	352	211	213		
	Yes	302 (25.7)	74 (21.0)	55 (26.1)	58 (27.2)	0.264	0.159
	No	872 (74.3)	278 (79.0)	156 (73.9)	155 (72.8)		
Currently Taking Calcium Channel Blockers	All	1,174	352	211	213		
	Yes	158 (13.5)	43 (12.2)	30 (14.2)	26 (12.2)	0.864	0.889
	No	1,016 (86.5)	309 (87.8)	181 (85.8)	187 (87.8)		
Currently Taking Diuretics	All	1,174	352	211	213		
	Yes	156 (13.3)	39 (11.1)	31 (14.7)	36 (16.9)	0.242	0.172
	No	1,018 (86.7)	313 (88.9)	180 (85.3)	177 (83.1)		

 *: Statistically significant (0.010<p-value≤0.050).
 **: Statistically significant (p-value≤0.010).

		Model 4		
		Correlation or Mean (n)	p-Value	
Covariate	Covariate Category	1987 Dioxin (ppt)	Unadjusted	Adjusted[a]
Body Mass Index (kg/m^2) (continuous)		775 r = 0.256	<0.001**	<0.001**
(discrete)	Not Obese (≤30)	O = 11.2 (501)	<0.001**	<0.001**
	Obese (>30)	O = 18.0 (274)		
Cholesterol (mg/dL) (continuous)	All	776 r = 0.009	0.813	0.230
(discrete)	0-200	O = 13.1 (438)	0.950	0.397
	>200-239	O = 13.5 (252)		
	>239	O = 13.1 (86)		
HDL (mg/dL) (continuous)	All	776 r = -0.180	<0.001**	0.003**
(discrete)	0-35	O = 15.2 (166)	0.067	0.372
	>35	O = 12.7 (610)		

		Model 4		
		Correlation or Mean (n)	p-Value	
Covariate	Covariate Category	1987 Dioxin (ppt)	Unadjusted	Adjusted[a]
Cholesterol-HDL Ratio (continuous)	All	776 r = 0.155	<0.001**	0.117
(discrete)	0-5	Ō = 12.1 (531)	<0.001**	0.268
	>5	Ō = 16.1 (245)		
Physical Activity Index	All	776		
	Sedentary	Ō = 15.6 (362)	<0.001**	0.011*
	Moderate	Ō = 11.3 (155)		
	Very Active	Ō = 11.5 (259)		
Diabetic Class[b]	All	776		
	Normal	Ō = 12.4 (466)	<0.001**	<0.001**
	Impaired	Ō = 11.8 (168)		
	Diabetic	Ō = 18.9 (142)		
Family History of Diabetes	All	768		
	Yes	Ō = 14.8 (244)	0.056	0.385
	No	Ō = 12.5 (524)		
Duration of Diabetes (years)[c] (continuous)	All	776 r = 0.146	<0.001**	<0.001**
(discrete)	0	Ō = 12.2 (655)	<0.001**	<0.001**
	>0	Ō = 20.1 (121)		
Family History of Heart Disease	All	770		
	Yes	Ō = 13.4 (498)	0.674	0.207
	No	Ō = 12.9 (272)		
Family History of Heart Disease Before Age 45	All	748		
	Yes	Ō = 13.0 (76)	0.863	0.291
	No	Ō = 13.3 (672)		
Uric Acid (mg/dL) (continuous)	All	776 r = 0.056	0.122	0.123
(discrete)	0-5.5	Ō = 12.4 (375)	0.125	0.153
	>5.5	Ō = 14.0 (401)		
Waist-to-Hip Ratio (continuous)	All	775 r = 0.200	<0.001**	<0.001**
(discrete)	0-1.0	Ō = 10.8 (404)	<0.001**	<0.001**
	>1.0	Ō = 16.5 (371)		
Currently Taking Blood Pressure Medication	All	776		
	Yes	Ō = 14.5 (344)	0.037*	0.025*
	No	Ō = 12.3 (432)		

Covariate	Covariate Category	Model 4		
		Correlation or Mean (n) 1987 Dioxin (ppt)	p-Value	
			Unadjusted	Adjusted[a]
Currently Taking Alpha- or Beta-Adrenergic Blocking Agents	All	776		
	Yes	O = 13.1 (167)	0.924	0.274
	No	O = 13.3 (609)		
Currently Taking ACE Inhibitors	All	776		
	Yes	O = 15.5 (187)	0.028*	0.055
	No	O = 12.6 (589)		
Currently Taking Calcium Channel Blockers	All	776		
	Yes	O = 12.9 (99)	0.820	0.918
	No	O = 13.3 (677)		
Currently Taking Diuretics	All	776		
	Yes	O = 15.4 (106)	0.129	0.126
	No	O = 12.9 (670)		

[a]Analyses are adjusted for military occupation.
[b]Diabetic Class:

Diabetic: past history of diabetes, as diagnosed previously by a physician, or $\geq$200 mg/dL 2-hour postprandial glucose on two separate occasions, or $\geq$126 mg/dL fasting glucose on two separate occasions, or one 2-hour postprandial glucose measurement $\geq$200 mg/dL and one fasting glucose $\geq$126 mg/dL on two separate occasions.

Impaired: not diabetic; $\geq$140 mg/dL 2-hour postprandial glucose or $\geq$110 mg/dL fasting glucose at the 2002 physical examination.

Normal: not diabetic or impaired; <140 mg/dL 2-hour postprandial glucose and <110 mg/dL fasting glucose at the 2002 physical examination.

[c]Nondiabetics and participants who were diagnosed as diabetic subsequent to the 2002 physical examination were assigned the value of 0 years for duration of diabetes.

*: Statistically significant (0.010<p-value$\leq$0.050).
**: Statistically significant (p-value$\leq$0.010).

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and for 1987 dioxin in Model 4.

8.7 SUN-EXPOSURE VARIABLES

Results of tests of association between a participant's reaction to sun exposure and the estimates of dioxin exposure are shown in Table 8-6. These statistics are based on non-Black participants because the sun-exposure covariates were used in only adjusted analyses of skin neoplasms and Blacks were excluded from those analyses.

No significant associations were seen between skin color and group in Model 1 or between skin color and initial dioxin in Model 2 unadjusted and adjusted analyses (p>0.06 for all analyses). In Model 3, the percentage of participants with peach skin color differed significantly among the Ranch Hands categorized by dioxin levels and Comparisons with or without adjustment for military occupation (p=0.034 unadjusted, p=0.018 adjusted). For Ranch Hands in the low dioxin category, 83.2 percent had peach skin color compared to 76.4 percent of Ranch Hands in the high dioxin category, 74.3 percent of Ranch Hands in the background category, and 73.3 percent of Comparisons. Participants with peach skin color had significantly higher mean 1987 dioxin levels (13.8 ppt) than participants with nonpeach skin color (11.7 ppt) in Model 4 only after adjustment for military occupation (p=0.103 unadjusted, p=0.008 adjusted).

A significant association between hair color and dioxin levels was observed in unadjusted Model 2 (p=0.002) and Model 3 (p=0.005) analyses, but was not seen in the unadjusted analyses of Model 1 (p=0.729) and Model 4 (p=0.056). After adjusting for military occupation, however, all associations in Model 1 through Model 4 analyses were not significant (p>0.07 for all analyses).

Eye color differed significantly between Ranch Hands and Comparisons in Model 1, before and after adjustment for military occupation (p=0.026 unadjusted, p=0.025 adjusted). Brown eyes and blue eyes were more prevalent in Comparisons than Ranch Hands (31.9 percent versus 27.5 percent for brown eyes; 42.6 percent versus 41.8 percent for blue eyes), but hazel and green eyes were less common in Comparisons than Ranch Hands (25.5 percent versus 30.8 percent). No other significant associations were seen in the unadjusted or adjusted analyses of Models 2, 3, and 4 (p>0.05 for all analyses).

No significant associations were observed between group or dioxin exposure estimates and reaction of skin to sun after at least 2 hours, reaction of skin to sun after repeated exposures, or the composite sun-reaction index for either the adjusted or unadjusted analyses (p>0.12 for all analyses).

Unadjusted and adjusted analyses of average lifetime residential latitude revealed significant associations with dioxin exposure in Model 1 (p=0.025 unadjusted, p=0.020 adjusted) and Model 2 (p=0.010 unadjusted, p=0.002 adjusted) unadjusted and adjusted analyses. In Model 1, significantly more Comparisons lived closer to the equator (53.6%), on average, than Ranch Hands (48.1%). In Model 2, the mean initial dioxin levels were greater for participants living closer to the equator (159.3 ppt) than for those living farther from the equator (125.0 ppt). No difference in average lifetime residential latitude was seen between Comparisons and the Ranch Hand dioxin categories in Model 3 unadjusted and adjusted analyses (p>0.06 for all analyses). While no significant association was seen in the unadjusted analysis of Model 4 (p=0.238), the association between latitude was significant when adjusting for military occupation (p=0.026). Participants living closer to the equator, on average, had higher mean 1987 dioxin levels (14.0 ppt) than participants living farther from the equator (12.7 ppt).

Table 8-6. Associations Between Sun-Exposure Variables and Estimates of Herbicide or Dioxin Exposure (Non-Blacks Only)

		Model 1			
		n (%)		p-Value	
Covariate	Covariate Category	Ranch Hand	Comparison	Unadjusted	Adjusted[a]
Skin Color	All	728	1,098		
	Peach	562 (77.2)	805 (73.3)	0.069	0.061
	Nonpeach	166 (22.8)	293 (26.7)		
Hair Color	All	728	1,098		
	Black, Dark Brown	505 (69.4)	752 (68.5)	0.729	0.684
	Light Brown, Blond, Red, Bald	223 (30.6)	346 (31.5)		
Eye Color	All	728	1,098		
	Brown	200 (27.5)	350 (31.9)	0.026*	0.025*
	Hazel, Green	224 (30.8)	280 (25.5)		
	Gray, Blue	304 (41.8)	468 (42.6)		
Reaction of Skin to Sun After at Least 2 Hours	All	728	1,096		
	No Reaction	235 (32.3)	354 (32.3)	0.756	0.762
	Becomes Red	332 (45.6)	496 (45.3)		
	Burns	114 (15.7)	186 (17.0)		
	Painfully Burns	47 (6.5)	60 (5.5)		
Reaction of Skin to Sun After Repeated Exposure	All	728	1,096		
	Tans Dark Brown	173 (23.8)	233 (21.3)	0.129	0.138
	Tans Moderately	382 (52.5)	616 (56.2)		
	Tans Mildly	139 (19.1)	214 (19.5)		
	Freckles with No Tan	34 (4.7)	33 (3.0)		
Composite Sun-Reaction Index	All	728	1,096		
	High	67 (9.2)	80 (7.3)	0.178	0.179
	Medium	173 (23.8)	292 (26.6)		
	Low	488 (67.0)	724 (66.1)		
Average Lifetime Residential Latitude	All	727	1,095		
	<37°	350 (48.1)	587 (53.6)	0.025*	0.020*
	≥37°	377 (51.9)	508 (46.4)		

*: Statistically significant (0.010<p-value≤0.050).

		Model 2		
		Mean (n)	p-Value	
Covariate	Covariate Category	Initial Dioxin (ppt)	Unadjusted	Adjusted[a]
Skin Color	All	393		
	Peach	O = 137.9 (313)	0.437	0.650
	Nonpeach	O = 151.0 (80)		

Covariate	Covariate Category	Model 2 Mean (n) Initial Dioxin (ppt)	p-Value Unadjusted	p-Value Adjusted[a]
Hair Color	All	393		
	Black, Dark Brown	O = 154.2 (277)	0.002**	0.245
	Light Brown, Blond, Red, Bald	O = 112.5 (116)		
Eye Color	All	393		
	Brown	O = 162.0 (114)	0.128	0.058
	Hazel, Green	O = 127.5 (122)		
	Gray, Blue	O = 136.6 (157)		
Reaction of Skin to Sun After at Least 2 Hours	All	393		
	No Reaction	O = 152.5 (124)	0.389	0.499
	Becomes Red	O = 138.5 (189)		
	Burns	O = 119.1 (58)		
	Painfully Burns	O = 154.1 (22)		
Reaction of Skin to Sun After Repeated Exposure	All	393		
	Tans Dark Brown	O = 149.6 (100)	0.867	0.826
	Tans Moderately	O = 136.7 (205)		
	Tans Mildly	O = 141.4 (70)		
	Freckles with No Tan	O = 131.1 (18)		
Composite Sun-Reaction Index	All	393		
	High	O = 153.5 (35)	0.769	0.995
	Medium	O = 134.3 (90)		
	Low	O = 141.0 (268)		
Average Lifetime Residential Latitude	All	393		
	<37°	O = 159.3 (189)	0.010**	0.002**
	≥37°	O = 125.0 (204)		

**: Statistically significant (p-value≤0.010).

		Model 3					
		n (%)				p-Value	
		Comparison	Ranch Hand				
Covariate	Covariate Category	Comparison	Background	Low	High	Unadjusted	Adjusted[a]
Skin Color	All	1,098	334	190	203		
	Peach	805 (73.3)	248 (74.3)	158 (83.2)	155 (76.4)	0.034*	0.018*
	Nonpeach	293 (26.7)	86 (25.8)	32 (16.8)	48 (23.7)		

Covariate	Covariate Category	Comparison	Background	Low	High	Unadjusted	Adjusted[a]
			Model 3				
			n (%)				
				Ranch Hand		**p-Value**	
		Comparison	**Background**	**Low**	**High**	**Unadjusted**	**Adjusted**[a]
Hair Color	All	1,098	334	190	203		
	Black, Dark Brown	752 (68.5)	227 (68.0)	118 (62.1)	159 (78.3)	0.005**	0.078
	Light Brown, Blond, Red, Bald	346 (31.5)	107 (32.0)	72 (37.9)	44 (21.7)		
Eye Color	All	1,098	334	190	203		
	Brown	350 (31.9)	86 (25.8)	47 (24.7)	67 (33.0)	0.068	0.141
	Hazel, Green	280 (25.5)	101 (30.2)	61 (32.1)	61 (30.1)		
	Gray, Blue	468 (42.6)	147 (44.0)	82 (43.2)	75 (37.0)		
Reaction of Skin to Sun After at Least 2 Hours	All	1,096	334	190	203		
	No Reaction	354 (32.3)	110 (32.9)	56 (29.5)	68 (33.5)	0.790	0.853
	Becomes Red	496 (45.3)	143 (42.8)	92 (48.4)	97 (47.8)		
	Burns	186 (17.0)	56 (16.8)	32 (16.8)	26 (12.8)		
	Painfully Burns	60 (5.5)	25 (7.5)	10 (5.3)	12 (5.9)		
Reaction of Skin to Sun After Repeated Exposure	All	1,096	334	190	203		
	Tans Dark Brown	233 (21.3)	72 (21.6)	44 (23.2)	56 (27.6)	0.360	0.550
	Tans Moderately	616 (56.2)	177 (53.0)	98 (51.6)	107 (52.7)		
	Tans Mildly	214 (19.5)	69 (20.7)	39 (20.5)	31 (15.3)		
	Freckles with No Tan	33 (3.0)	16 (4.8)	9 (4.7)	9 (4.4)		
Composite Sun-Reaction Index	All	1,096	334	190	203		
	High	80 (7.3)	32 (9.6)	15 (7.9)	20 (9.9)	0.498	0.374
	Medium	292 (26.6)	83 (24.9)	48 (25.3)	42 (20.7)		
	Low	724 (66.1)	219 (65.6)	127 (66.8)	141 (69.5)		
Average Lifetime Residential Latitude	All	1,095	333	190	203		
	<37°	587 (53.6)	160 (48.0)	86 (45.3)	103 (50.7)	0.088	0.068
	≥37°	508 (46.4)	173 (52.0)	104 (54.7)	100 (49.3)		

*: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Covariate	Covariate Category	Mean (n) 1987 Dioxin (ppt)	Unadjusted	Adjusted[a]
		Model 4		
		Mean (n) 1987 Dioxin (ppt)	**p-Value**	
			Unadjusted	**Adjusted**[a]
Skin Color	All	727		
	Peach	Õ = 13.8 (561)	0.103	0.008**
	Nonpeach	Õ = 11.7 (166)		

Covariate	Covariate Category	Model 4		
		Mean (n) 1987 Dioxin (ppt)	p-Value	
			Unadjusted	Adjusted[a]
Hair Color	All	727		
	Black, Dark Brown	O = 14.0 (504)	0.056	0.969
	Light Brown, Blond, Red, Bald	O = 11.8 (223)		
Eye Color	All	727		
	Brown	O = 15.1 (200)	0.164	0.275
	Hazel, Green	O = 12.7 (223)		
	Gray, Blue	O = 12.6 (304)		
Reaction of Skin to Sun After at Least 2 Hours	All	727		
	No Reaction	O = 13.1 (234)	0.334	0.254
	Becomes Red	O = 14.2 (332)		
	Burns	O = 11.5 (114)		
	Painfully Burns	O = 12.1 (47)		
Reaction of Skin to Sun After Repeated Exposure	All	727		
	Tans Dark Brown	O = 14.2 (172)	0.735	0.959
	Tans Moderately	O = 13.3 (382)		
	Tans Mildly	O = 12.4 (139)		
	Freckles with No Tan	O = 12.3 (34)		
Composite Sun-Reaction Index	All	727		
	High	O = 13.2 (67)	0.639	0.594
	Medium	O = 12.4 (173)		
	Low	O = 13.6 (487)		
Average Lifetime Residential Latitude	All	726		
	<37°	O = 14.0 (349)	0.238	0.026*
	≥37°	O = 12.7 (377)		

[a]Analyses are adjusted for military occupation.

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and for 1987 dioxin in Model 4.

8.8   OTHER MISCELLANEOUS COVARIATES

Results of tests of association between other miscellaneous covariates and the estimates of dioxin exposure are shown in Table 8-7. Examining the association between current total household income in its continuous form and dioxin yielded significant results in the analysis of Models 2 through 4 ($p<0.001$ for all analyses). When adjusted for military occupation, the association between income and dioxin levels was not significant for any of the models ($p>0.15$ for each analysis). The current income of Ranch Hands was not significantly different than Comparisons in Model 1 unadjusted and adjusted analyses, even after adjustment for military occupation ($p>0.41$ for all analyses).

When income was categorized, significant associations were seen between current income and dioxin exposure in the unadjusted analysis of Model 2, Model 3, and Model 4 ($p=0.005$ for Model 2; $p=0.007$ for Model 3; $p=0.013$ for Model 4). Model 2 and Model 3 results were not significant after adjustment for military occupation ($p>0.25$ for each analysis). Model 4 results, however, remained significant after adjusting for military occupation ($p=0.022$). The mean 1987 dioxin level was higher in participants making less than \$65,000 per year (14.8 ppt) than in participants with higher incomes (12.1 ppt). No significant difference in current income was seen between Ranch Hands and Comparisons in Model 1 analyses ($p>0.36$ for all analyses).

The relation between education and group was not significant in Model 1 unadjusted and adjusted analyses ($p>0.24$ for all analyses). A significant relation between education and dioxin was revealed for Models 2 through 4 ($p\leq0.001$ for each model). After adjusting for military occupation, however, no significant relations were observed in Models 2, 3, or 4 ($p>0.28$ for all analyses).

No significant relation between current employment status and dioxin exposure was seen in Model 1, Model 2, or Model 3 unadjusted and adjusted analyses ($p>0.05$ for all analyses). Significant relations were seen between 1987 dioxin levels and current employment status in Model 4 in the unadjusted analysis ($p=0.031$), but the relations were no longer significant when adjusted for military occupation ($p=0.271$).

In the analysis of the relation between current marital status and dioxin exposure, no significant association was observed in Model 1, Model 2, or Model 3 unadjusted and adjusted analyses ($p>0.08$ for all analyses). A significant relation between current marital status and 1987 dioxin levels was seen in the unadjusted analysis of Model 4 ($p=0.049$). After adjusting for military occupation, however, the relation was no longer significant ($p=0.527$).

Current parental status (having a child younger than 18 years old at home) was not significantly related to dioxin exposure estimates in Model 1 through Model 4 unadjusted and adjusted analyses ($p>0.09$ for all analyses).

The analysis of participants who reported having worked with vibrating power equipment or tools for 30 days or more revealed a significant association with 1987 dioxin ($p=0.019$) in Model 4. After adjustment for military occupation, however, this association was not significant ($p=0.581$). All tests of association in Model 1 through Model 3 were not significant for this covariate ($p\geq0.07$ for all analyses).

Tests of the association between reported exposure to heavy metals (worked for 30 days or more with lead, mercury, chromium, nickel, copper, cadmium, manganese, arsenic, selenium, or molybdenum) and dioxin were significant for categorized dioxin in Model 3 ($p=0.011$) and 1987 dioxin in Model 4 ($p=0.011$). After adjustment for military occupation, the association was not significant in Model 3 ($p=0.321$) or in Model 4 ($p=0.621$). All tests of association between reported exposure to heavy metals

and group in Model 1 unadjusted and adjusted analyses were not significant (p>0.09 for all analyses), as were tests of association between reported exposure to heavy metals and initial dioxin in Model 2 unadjusted and adjusted analyses (p>0.23 for all analyses).

No significant associations were seen between dioxin exposure and the length of exercise prior to peripheral blood pressure measurements in the continuous or discrete forms for Model 1 through Model 4 unadjusted and adjusted analyses (p>0.46 for all analyses).

Table 8-7. Associations Between Other Miscellaneous Covariates and Estimates of Herbicide or Dioxin Exposure

| Covariate | Covariate Category | Model 1 | | | |
| | | Mean or n (%) | | p-Value | |
		Ranch Hand	Comparison	Unadjusted	Adjusted[a]
Current Total Household Income (dollars)	All	757	1,139		
(continuous)		Ō = $68,623	Ō = $69,638	0.424	0.413
(discrete)	<$65,000	355 (46.9)	510 (44.8)	0.390	0.369
	≥$65,000	402 (53.1)	629 (55.2)		
Education	All	777	1,172		
	High School	369 (47.5)	531 (45.3)	0.368	0.241
	College	408 (52.5)	641 (54.7)		
Current Employment Status	All	776	1,172		
	Yes	430 (55.4)	656 (56.0)	0.844	0.906
	No	346 (44.6)	516 (44.0)		
Current Marital Status	All	777	1,171		
	Married	653 (84.0)	992 (84.7)	0.736	0.664
	Not Married	124 (16.0)	179 (15.3)		
Current Parental Status (Child Younger than 18 Years of Age Living at Home)	All	777	1,172		
	Yes	68 (8.8)	119 (10.2)	0.342	0.323
	No	709 (91.3)	1,053 (89.9)		
Worked with Vibrating Power Equipment or Tools	All	775	1,172		
	Yes	229 (29.6)	324 (27.7)	0.390	0.339
	No	546 (70.5)	848 (72.4)		
Composite Exposure to Heavy Metals	All	774	1,167		
	Yes	103 (13.3)	188 (16.1)	0.104	0.099
	No	671 (86.7)	979 (83.9)		
Length of Exercise Prior to Peripheral Blood Pressure Measurements (seconds)	All	750	1,129		
(continuous)		Ō = 118.3	Ō = 117.9	0.467	0.461
(discrete)	<120	33 (4.4)	51 (4.5)	0.995	0.905
	120	717 (95.6)	1,078 (95.5)		

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Table 8-7. Associations Between Other Miscellaneous Covariates and Estimates of Herbicide or Dioxin Exposure (Continued)

Covariate	Covariate Category	Model 2 Correlation or Mean (n) Initial Dioxin (ppt)	p-Value Unadjusted	p-Value Adjusted[a]
Current Total Household Income (dollars) (continuous)	All	412 r = -0.191	<0.001**	0.154
(discrete)	<$65,000	O = 157.4 (207)	0.005**	0.516
	≥$65,000	O = 121.8 (205)		
Education	All	424		
	High School	O = 154.9 (247)	0.001**	0.286
	College	O = 114.9 (177)		
Current Employment Status	All	423		
	Yes	O = 146.8 (247)	0.056	0.364
	No	O = 123.3 (176)		
Current Marital Status	All	424		
	Married	O = 131.9 (347)	0.085	0.090
	Not Married	O = 161.1 (77)		
Current Parental Status (Child Younger than 18 Years of Age Living at Home)	All	424		
	Yes	O = 171.7 (41)	0.097	0.437
	No	O = 133.4 (383)		
Worked with Vibrating Power Equipment or Tools	All	423		
	Yes	O = 154.2 (135)	0.070	0.796
	No	O = 129.5 (288)		
Composite Exposure to Heavy Metals	All	422		
	Yes	O = 154.0 (68)	0.235	0.955
	No	O = 133.2 (354)		
Length of Exercise Prior to Peripheral Blood Pressure Measurements (seconds) (continuous)	All	405 r = 0.016	0.746	0.701
(discrete)	<120	O = 137.2 (20)	0.954	0.969
	120	O = 135.5 (385)		

**: Statistically significant (p-value≤0.010).

Table 8-7. Associations Between Other Miscellaneous Covariates and Estimates of Herbicide or Dioxin Exposure (Continued)

		Model 3					
		Mean or n (%)				p-Value	
				Ranch Hand			
Covariate	Covariate Category	Comparison	Background	Low	High	Unadjusted	Adjusted[a]
Current Total Household Income (dollars)	All	1,139	344	202	210		
(continuous)		Ō = $69,638	Ō = $72,253	Ō = $70,149	Ō = $61,357	<0.001**	0.522
(discrete)	<$65,000	510 (44.8)	147 (42.7)	88 (43.6)	119 (56.7)	0.007**	0.252
	≥$65,000	629 (55.2)	197 (57.3)	114 (56.4)	91 (43.3)		
Education	All	1,172	352	211	213		
	High School	531 (45.3)	121 (34.4)	103 (48.8)	144 (67.6)	<0.001**	0.581
	College	641 (54.7)	231 (65.6)	108 (51.2)	69 (32.4)		
Current Employment Status	All	1,172	352	211	212		
	Yes	656 (56.0)	183 (52.0)	113 (53.6)	134 (63.2)	0.065	0.992
	No	516 (44.0)	169 (48.0)	98 (46.5)	78 (36.8)		
Current Marital Status	All	1,171	352	211	213		
	Married	992 (84.7)	305 (86.7)	178 (84.4)	169 (79.3)	0.134	0.729
	Not Married	179 (15.3)	47 (13.4)	33 (15.6)	44 (20.7)		
Current Parental Status (Child Younger than 18 Years of Age Living at Home)	All	1,172	352	211	213		
	Yes	119 (10.2)	26 (7.4)	16 (7.6)	25 (11.7)	0.210	0.709
	No	1,053 (89.9)	326 (92.6)	195 (92.4)	188 (88.3)		
Worked with Vibrating Power Equipment or Tools	All	1,172	351	210	213		
	Yes	324 (27.7)	93 (26.5)	61 (29.1)	74 (34.7)	0.157	0.601
	No	848 (72.4)	258 (73.5)	149 (71.0)	139 (65.3)		
Composite Exposure to Heavy Metals	All	1,167	351	210	212		
	Yes	188 (16.1)	34 (9.7)	29 (13.8)	39 (18.4)	0.011*	0.321
	No	979 (83.9)	317 (90.3)	181 (86.2)	173 (81.6)		

		Model 3					
		Mean or n (%)				p-Value	
				Ranch Hand			
Covariate	Covariate Category	Comparison	Background	Low	High	Unadjusted	Adjusted[a]
Length of Exercise Prior to Peripheral Blood Pressure Measurements (seconds)	All	1,129	344	204	201		
(continuous)		Ō = 117.9	Ō = 118.3	Ō = 118.3	Ō = 118.2	0.905	0.909
(discrete)	<120	51 (4.5)	13 (3.8)	9 (4.4)	11 (5.5)	0.834	0.935
	120	1,078 (95.5)	331 (96.2)	195 (95.6)	190 (94.5)		

*: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

| | | Model 4 | | |
| | | Correlation or Mean (n) | p-Value | |
Covariate	Covariate Category	1987 Dioxin (ppt)	Unadjusted	Adjusted[a]
Current Total Household Income (dollars)		756		
(continuous)		r = -0.144	<0.001**	0.260
(discrete)	<$65,000	Ō = 14.8 (354)	0.013*	0.022*
	≥$65,000	Ō = 12.1 (402)		
Education	All	776		
	High School	Ō = 17.6 (368)	<0.001**	0.332
	College	Ō = 10.2 (408)		
Current Employment Status	All	775		
	Yes	Ō = 14.3 (430)	0.031*	0.271
	No	Ō = 12.0 (345)		
Current Marital Status	All	776		
	Married	Ō = 12.8 (652)	0.049*	0.527
	Not Married	Ō = 15.9 (124)		
Current Parental Status (Child Younger than 18 Years of Age Living at Home)	All	776		
	Yes	Ō = 16.4 (67)	0.104	0.821
	No	Ō = 13.0 (709)		
Worked with Vibrating Power Equipment or Tools	All	774		
	Yes	Ō = 15.3 (228)	0.019*	0.581
	No	Ō = 12.5 (546)		

| | | Model 4 | | |
| | Covariate | Correlation or Mean (n) | p-Value | |
Covariate	Category	1987 Dioxin (ppt)	Unadjusted	Adjusted[a]
Composite Exposure to Heavy Metals	All	773		
	Yes	O = 17.1 (102)	0.011*	0.621
	No	O = 12.7 (671)		
Length of Exercise Prior to Peripheral Blood Pressure Measurements (seconds) (continuous)	All	749 r = 0.022	0.546	0.675
(discrete)	<120	O = 13.3 (33)	0.917	0.795
	120	O = 13.1 (716)		

[a]Analyses are adjusted for military occupation.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: Means for discrete covariates were transformed from the logarithmic (base 2) scale for initial dioxin in Model 2 and for 1987 dioxin in Model 4.

8.9   SUMMARY

This chapter investigates whether the covariates used throughout this report were associated with the estimates of herbicide or dioxin exposure. Military occupation, being associated with education, may have influenced the associations between covariates and dioxin estimates. Therefore, associations between covariates and the estimates of exposure in this chapter were adjusted for military occupation but not for other known or suspected confounders. Associations between covariates and dioxin estimates should be interpreted with caution and do not necessarily reflect a causal relation.

The demographic variables of age, race, and military occupation were used as matching variables in the original study design. As expected because of the matching, there were no significant differences between Ranch Hands and Comparisons for these three variables. As exhibited in previous reports, dioxin was significantly associated with military occupation. Officers had the lowest levels, followed by enlisted flyers and enlisted groundcrew. Because the Ranch Hand enlisted groundcrew tended to be younger on average than the Ranch Hand officers and enlisted flyers and were more likely to have been exposed to dioxin, a strong inverse association was seen between dioxin levels and age. When military occupation was taken into consideration, however, initial and 1987 dioxin levels did not appear to be related to age. Race exhibited significant associations with dioxin in that Black participants appeared to have lower dioxin levels than non-Black participants. The association between race and serum dioxin levels was strengthened when military occupation was considered.

Lifetime alcohol consumption had a positive association with initial dioxin. A greater percentage of Comparisons than Ranch Hands were wine-drinkers and the percentage of wine-drinkers within the Ranch Hand group decreased as dioxin increased.

Significant associations were observed between current cigarette smoking and lifetime cigarette smoking history and 1987 dioxin after adjustment for military occupation.

Questions posed to the participants regarding exposure to known carcinogens were intended to indicate post-SEA exposures; however, the data suggest that the participants may have included SEA exposures as well. A greater percentage of Ranch Hands reported herbicide and insecticide exposure, which may indicate that Ranch Hands were more likely to report SEA or pre-SEA exposures than Comparisons. Significant associations were seen between dioxin and both degreasing chemicals and industrial chemicals, but adjusted analysis showed that these associations were related to military occupation. It is believed that fewer officers were exposed to industrial chemicals and degreasing chemicals than enlisted personnel. The percentage of Comparisons exposed to ionizing radiation was greater than the percentage of Ranch Hands exposed and did not appear to be related to military occupation.

The significant associations between dioxin and health measurements, such as body mass index, HDL cholesterol, physical activity level, diabetic class, duration of diabetes, and waist-to-hip ratios are likely to be explained by body fat. Higher body fat measurements are known to correspond to higher dioxin levels, lower levels of HDL cholesterol, and higher cholesterol-HDL ratios. In addition, higher body fat is more likely to occur with sedentary lifestyles and a higher waist-to-hip ratio. The relation between measures associated with diabetes and dioxin exposure is analyzed in detail in Chapter 18, Endocrinology Assessment.

Of covariates related to sun exposure, the relation between dioxin and hair color was significant, but could be explained by military occupation. Eye color differed between Ranch Hands and Comparisons in that more Comparisons had brown eyes, but no difference between groups was seen in 1987 or initial dioxin levels. More Ranch Hands had peach skin color than Comparisons and Ranch Hands with peach skin color had higher 1987 dioxin levels than Ranch Hands with a nonpeach skin color. On average, a greater percentage of Comparisons lived in latitudes closer to the equator than did Ranch Hands and higher levels of dioxin were seen for those Ranch Hands who live in latitudes closer to the equator. No significant associations were observed with the reaction to sun-exposure covariates.

Any relation between dioxin and current total household income, education, current employment status, current marital status, and having a child younger than 18 years old living at home appeared to be directly related to military occupation. Participants who were officers at the time of service in SEA were more likely to have higher current incomes than participants who were enlisted at the time of service in SEA. Officers had the lowest dioxin levels (Table 8-1); consequently, there was an inverse association between income and dioxin. A greater percentage of officers tended to be college graduates than enlisted personnel, and, consequently, college graduates had lower dioxin levels than participants with at most a high school diploma. Current marital and parental status may be related to military occupation directly or indirectly through the relation between military occupation and socioeconomic factors. No associations were seen between dioxin exposure and working with vibrating power equipment, exposure to heavy metals, or length of exercise prior to blood pressure measurements.

8.10 CONCLUSION

This chapter investigates whether the covariates used throughout this report were associated with herbicide or dioxin exposure and, therefore, could potentially be confounding variables in subsequent statistical analyses. Military occupation, being associated with education, may have influenced the associations between covariates and dioxin estimates. The associations between covariates and the estimates of dioxin exposure in this chapter were adjusted for military occupation, but not for other

known or suspected confounders. Therefore, associations between covariates and dioxin estimates should be interpreted with caution.

In general, the Ranch Hand and Comparison groups were similar for the majority of the covariates, with the following exceptions: current cigarette smoking, lifetime wine use, physical activity levels, uric acid levels, herbicide exposure, insecticide exposure, ionizing radiation exposure, eye color, and average lifetime residential latitude. A greater percentage of Ranch Hands than Comparisons reported herbicide exposure. Although the questionnaire had been structured to indicate post-SEA exposure only, a possible explanation for this association between group and herbicide exposure may have been the tendency of Ranch Hands to report their exposure to dioxin during their time of duty in SEA. A greater percentage of Ranch Hands reported exposure to insecticides than did Comparisons, and more Comparisons reported ionizing radiation exposure. More Comparisons had a history of wine use than Ranch Hands. Ranch Hands had a higher average level of current cigarette use than Comparisons. More Comparisons than Ranch Hands lived in latitudes closer to the equator. Ranch Hands who lived closer to the equator had a higher average initial and 1987 dioxin level than Ranch Hands living farther from the equator.

Most of the significant associations between dioxin and the covariates in the Ranch Hand group can be explained at least partially by the associations between dioxin and military occupation or body mass index. Of the three military occupational cohorts, enlisted groundcrew had the highest levels of 1987 and initial dioxin. Adjusted analyses in the clinical chapters fully account for group, age, military occupation, and other potential confounders to further investigate significant associations between covariates and dioxin. Body mass index and the half-life of dioxin are known to be related; consequently, the Models 2 and 3 analyses in the clinical chapters were adjusted for body mass index. In addition, body mass index was used as a risk factor where appropriate. The reader is referred to the clinical chapters for a more complete assessment of the associations between dioxin and relevant medical endpoints.

REFERENCE

1.   Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L. R. Alexander, and
      L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric
      analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-
      p-dioxin. *Annals of Chemistry* 59:2000-5.

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9   GENERAL HEALTH ASSESSMENT

9.1   INTRODUCTION

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9.1.1.1   Organs/Diseases

Four variables were included in the Air Force Health Study (AFHS) general health assessment: self-perception of health, appearance of illness or distress during the examination, relative age, and body mass index. For the evaluation of self-perception of health, each participant was asked to rate his health (excellent, good, fair, poor) compared to other people his age. In addition, a board-certified internist examined the participants for the appearance of acute illness or distress (yes or no). The internist assessed whether each subject appeared younger than, older than, or the same as his stated age to determine relative age. Body mass index was computed based on height and weight recorded at the physical examination. Erythrocyte sedimentation rate had been discussed under the general health assessment for previous AFHS examination reports, but this laboratory parameter is in the hematology assessment (see Chapter 16).

9.1.1.2   Toxicology

The assessment of the risk of dioxin exposure to human health is in large part based on the molecular and cellular mechanisms of dioxin toxicity in animals and has been the subject of numerous review articles (1-8). In laboratory animals, dioxin toxicity is species- and strain-specific and appears to correlate with the presence of a stereospecific protein receptor, the aryl hydrocarbon (Ah) receptor, found in the cytosol of selected organs and capable of binding aromatic hydrocarbons (9-12). Ah receptors have been isolated in the tissue of several human organs (12-17), and the comparative properties of animal and human Ah receptors have been studied (18, 19). A recent literature review concluded that toxicological data continue to support the role of the Ah receptor in dioxin toxicity, and the biological plausibility of endpoints of toxicity in humans similar to those found in animals (20). The exact mechanistic basis of the differences in toxicity found across species and tissue types, however, is not known (20). Nevertheless, these studies of animal toxicology and the presence of the Ah receptor in humans form the basis for several epidemiologic studies that evaluate the association between dioxin exposure and numerous health outcomes.

9.1.1.3   Epidemiology

Although the potentially lethal consequences of acute phenoxy herbicide toxication in humans have been well-defined (21, 22), the long-term effects of herbicide exposure on human health remain controversial. Epidemiologic studies of such long-term health effects published in scientific literature have focused on target organ effects defined in animal models, including immunotoxicity, carcinogenicity, hepatotoxicity, and neurotoxicity. These epidemiologic studies were based on cohorts of Vietnam veterans (23-47), civilian populations occupationally exposed to dioxins (48-79), or consequences of industrial accidents (68, 80-90). Such studies were reviewed comprehensively (20, 91-97), and were considered in detail in subsequent chapters of this report.

Exposure assessments in early investigations of human health effects of herbicides relied on job titles or production processes from work history records, occupations from death certificates, cancer registries or hospital records, job tasks or exposure status based on self-reports, or residential locations. The lack of an accurate measure of exposure is recognized as the most important methodological limitation common to all of these studies (91).

Assay techniques developed in 1987 by the Centers for Disease Control and Prevention (CDC) (98) permitted the accurate detection and quantitative measurement of trace amounts of dioxin in blood and adipose tissue and the identification of subjects with prior exposure to dioxin. The CDC's study of serum dioxin levels demonstrated that there was no significant difference in the current body burden of dioxin between most Vietnam and non-Vietnam veterans of the same era (99, 100). Nevertheless, it has been shown that of all veterans who served in Vietnam, the Air Force Ranch Hand personnel were among those exposed most highly to dioxin and that, within this group, the enlisted groundcrew responsible for handling the herbicides and for maintaining the spray equipment were at the greatest risk for exposure (26, 27, 101).

Analyses of serum dioxin data from the AFHS (102, 103) and several other epidemiologic studies (67, 104-106) were published and have contributed to a better understanding of the pharmacokinetics of dioxin in humans. The reliability and reproducibility of the serum dioxin assay were established (107) and the potential effects of age, body fat, and time since exposure on the rate of dioxin elimination were explored (102). These recent analyses confirmed an earlier report (108) that an increase in body fat is associated with prolongation of the dioxin half-life, a finding that may be relevant to the development of clinical endpoints related to obesity. Based on the pharmacokinetic analyses of serial serum dioxin levels taken from Ranch Hand veterans and subjects exposed to dioxin after an industrial accident, the half-life of dioxin in humans is estimated to be 7.6 years (45). Dioxin was observed to be more rapidly eliminated within the first few months of exposure among individuals who were briefly exposed (44).

The importance of the serum dioxin assay is reflected in the number of publications reporting serum dioxin levels in exposed populations around the world, including the United States (49, 77, 101, 103, 109-114), Asia (78, 79, 115, 116), Germany (117-119), Russia (76, 120, 121), New Zealand (122), Austria (123), Australia (124), and Italy (86, 106, 125).

In response to unanswered questions and ongoing concerns that Vietnam veterans may have been harmed by herbicide defoliants, Congress passed the Agent Orange Act of 1991 in February 1991. Under this legislation, Public Law 102-4, the National Academy of Sciences, Institute of Medicine (IOM), was mandated to conduct an independent review of all scientific evidence relevant to the issue of health effects of Agent Orange, and to make recommendations for the directions of future research. The first IOM report (91), *Veterans and Agent Orange*, was published in 1994, with biennial updates published in 1996, 1998, 2000, and 2002 (20, 92, 96, 97). These reports provide a comprehensive resource of information on the potential health consequences of exposure to herbicides and, particularly, to the contaminant dioxin. Among the valuable contributions of the IOM reports (20) is the assessment of the scientific evidence for and against a statistical association with herbicide or dioxin exposure according to four categories: (1) sufficient evidence of an association, (2) limited or suggestive evidence of an association, (3) inadequate or insufficient evidence to determine whether an association exists, and (4) limited or suggestive evidence of no association. The committee established by the IOM concentrated its efforts on epidemiologic studies to evaluate the statistical association (20).

The committee in 1994 emphasized the merits of the model of the AFHS and proposed that a similar methodology be applied to a study of the only other veteran group with significant herbicide exposure—

the Army Chemical Corps (91). In the first IOM report (91), the committee endorsed the continued follow-up of the Air Force Ranch Hand and Comparison cohorts.

In the 1982, 1985, 1992, and 1997 AFHS examinations, dioxin-exposed cohort members perceived themselves to be in poorer health than unexposed participants (23, 24, 27, 34). No differences were noted in the appearance of illness or relative age (34). In the 1987, 1992, and 1997 examinations, a positive association was observed between obesity and the serum dioxin level (26, 27, 34). Apart from the AFHS examinations, only a few published reports related clinical and laboratory indices other than those described above to serum or adipose dioxin levels (49, 66, 68, 87, 126-129). These studies, which related specific health outcomes with evidence of prior exposure to dioxin, are discussed in subsequent chapters.

9.1.2   Summary of Previous Analyses of the AFHS

9.1.2.1   *1982 Baseline Examination Summary Results*

General health variables for the 1982 baseline examination included self-perception of health, appearance of illness or distress, relative age, and body fat. A statistically significant difference in self-perception of health was found between the Ranch Hand and Comparison groups, with a greater percentage of Ranch Hands reporting their health as fair or poor than Comparisons (20.6% versus 14.2%). This was true in both the younger and older age groups. Because only 9 (8 Ranch Hands) of 1,811 individuals were reported by the examining physician as appearing ill or distressed, this designation was apparently reserved for only very ill or distressed individuals. Conversely, more Ranch Hands than Comparisons were reported by the examiners as appearing younger than their actual ages (4.9% versus 2.5%, p=0.029). No overall differences in body fat were found.

9.1.2.2   *1985 Follow-up Examination Summary Results*

General physical health was evaluated by the same measures used in the baseline examination (self-perception of health, appearance of illness or distress, relative age, and body fat). The Ranch Hands again rated their health as fair or poor more often than the Comparisons (9.1% versus 7.3%, respectively), although this difference was not statistically significant. Further analysis revealed a significant group-by-occupation interaction. Differences were largely confined to the enlisted groundcrew category where the adjusted relative risk was 1.90 (p=0.003).

Ten individuals were reported as appearing acutely ill or distressed at the 1985 follow-up examination. In contrast to the baseline examination, four were Ranch Hands and six were Comparisons; thus, no group difference was suggested. Relative age, as determined by the examining physician, was not significantly different in the two groups.

The mean body fat of the Ranch Hands was significantly lower than the Comparisons (21.10 percent versus 21.54 percent, p=0.037), and the difference was of nearly the same magnitude after adjustment for age, race, and occupation.

Longitudinal differences between the 1982 baseline and the 1985 follow-up examination were assessed by analyses of self-perception of health. Analysis of self-perception of health showed no significant group differences in the change over time, with the Ranch Hand and Comparison groups reporting symmetrical improvements in their perceptions over the 3-year period.

9.1.2.3   1987 Follow-up Examination Summary Results

The general health in the Ranch Hand and Comparison groups was assessed by the same measures used in previous AFHS examinations: self-perception of health, appearance of illness or distress, relative age, and body fat. There were no significant group differences nor were there any significant group-by-covariate interactions for self-perception of health, appearance of illness or distress, relative age, or percent body fat. Longitudinal analyses revealed a similar decline in both groups over time in the percentage of individuals reporting their health as fair or poor.

9.1.2.4   Serum Dioxin Analysis of 1987 Follow-up Examination Summary Results

Body fat exhibited a significant positive association with initial dioxin. The adjusted analysis of relative age appearance exhibited significant interactions between dioxin and time since tour of duty. For Ranch Hands with 18.6 years or less since the end of duty in Southeast Asia (SEA), the associations between relative age and dioxin were positive and significant for the adjusted analysis under the minimal exposure assumption (i.e., Ranch Hands with less than or equal to 10 ppt of dioxin, as measured in 1987, were not used). For the other variables, the dioxin-by-time analyses generally displayed nonsignificant but positive associations with dioxin.

In general, the adjusted analyses for the four dioxin categories overall exhibited significant contrasts for body fat, with Ranch Hands exceeding Comparisons for the high versus background contrast and the low versus background contrast. The body fat results of dioxin in its categorized form displayed an increasing association with dioxin within the Ranch Hands (i.e., unknown [termed as "background" in subsequent reports], low, and high categories); however, the background category for Comparisons exceeded the unknown category for Ranch Hands.

The longitudinal analyses of self-perception of health demonstrated significant positive associations with dioxin. The percentage of participants who reported fair or poor health decreased by more than 50 percent from 1982 to 1987.

9.1.2.5   1992 Follow-up Examination Summary Results

In the assessment of general health, significant differences between Ranch Hands and Comparisons—the enlisted groundcrew in particular—were evident for self-perception of health. Significant associations between negative self-perception of health and levels of dioxin also were evident. These results were consistent with the 1985 and 1987 follow-up examinations. In contrast to self-perception of health, no significant results were found for the appearance of illness or distress and relative age appearance, which were recorded by the examining physicians. The analyses of body fat displayed a significant positive association with dioxin, whether calculated on a whole-weight or lipid-adjusted basis.

In the longitudinal analysis, the increase in the percentage of Ranch Hands who perceived their health to be poor in 1992 from those that were normal in 1982 was significantly associated with initial dioxin levels. Relative age appearance also displayed a significant positive association with initial dioxin. The change in body fat from 1982 to 1992 was significantly associated with initial dioxin, and a significant difference between Ranch Hands and Comparisons also was found, especially in enlisted groundcrew.

9.1.2.6   1997 Follow-up Examination Summary Results

The self-perception of health analysis revealed significant differences among Ranch Hands and Comparisons, with more Ranch Hands than Comparisons indicating their health as fair or poor. As in previous examinations, the difference was most apparent in enlisted groundcrew, who had the highest

median dioxin level. This observation also was confirmed in the categorized dioxin analysis, where Ranch Hands with the highest dioxin levels perceived their health as fair or poor more often than Comparisons. Also, among Ranch Hands, those with the higher 1987 dioxin levels reported fair or poor health more often than Ranch Hands with lower levels. These results were consistent with the 1985, 1987, and 1992 examinations. No group differences were noted in the appearance of illness or relative age, as recorded by examining physicians, nor were these variables correlated with serum dioxin levels in the Ranch Hand cohort.

The analysis of body fat indicated positive associations with dioxin levels. The results of the 1997 examination confirmed those of the 1992 examination and appear consistent with a difference in dioxin pharmacokinetics in obese versus lean individuals.

In conclusion, fair or poor self-perception of health displayed an adverse association with dioxin. Increased body fat was associated with increased levels of dioxin exposure, a finding most likely related to the pharmacokinetics of dioxin elimination. Other measures of general health revealed no association with levels of dioxin.

9.1.3   Parameters for the 2002 General Health Assessment

9.1.3.1   Dependent Variables

The general health assessment was based on data from the 2002 questionnaire and physical examination.

9.1.3.1.1   Questionnaire Variable

During the health interview administered through the 2002 National Opinion Research Center (NORC) questionnaire, each AFHS participant was asked the following: "Compared to other people your age, would you say your health is excellent, good, fair, or poor?" This self-reported perception was analyzed as a measure of the general health status of each participant, although it was recognized that the perception was susceptible to varying degrees of conscious and subconscious bias (e.g., most participants were aware of their serum dioxin levels). This variable was dichotomized as "excellent or good" and "fair or poor" for statistical analyses. No participants were excluded for medical reasons from the analysis of this variable.

9.1.3.1.2   Physical Examination Variables

Three variables derived from the 2002 Scripps Clinic physical examination were analyzed in the assessment of general health. For the first variable, the board-certified internist at the examination recorded the appearance of acute illness or distress (yes, no) of the AFHS participant. For the second variable, the internist noted the appearance of the subject as younger than, older than, or the same as his stated age. This variable was dichotomized as "older than" and "same as or younger than" for statistical analyses. Because the examining internist was kept blind to the participant's group membership, these assessments were less subject to bias than the self-perception of health.

The third variable, body mass index, was calculated as weight/(height)^2, where the weight was measured in kilograms and the height was measured in meters at the physical examination (130). This variable was analyzed in both the discrete and continuous forms. For purposes of discrete analyses, body mass index was dichotomized as "not obese" (≤ 30 kg/m^2) and "obese" (>30 kg/m^2). Underweight participants (<18.5 kg/m^2) and participants with a normal body mass index (131) were combined into one category because only four participants (two Ranch Hand, two Comparison) fit this definition. This variable does not

reflect changes in weight since time of duty in SEA. No participants were excluded for medical reasons from the analyses of these three variables.

9.1.3.2 Covariates

The effects of the covariates age (in years), race (Black, non-Black), military occupation (officer, enlisted flyer, enlisted groundcrew), current cigarette smoking (cigarettes/day), lifetime cigarette smoking history (pack-years), current alcohol use (drinks/day), and lifetime alcohol history (drink-years) were used for analyses with all dependent variables.

Age, race, and military occupation were determined from military records. Lifetime alcohol history was based on information from the 2002 questionnaire and combined with similar information gathered at the 1987, 1992, and 1997 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking pattern changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year. Current alcohol use was defined as the average number of drinks per day during the 2 weeks prior to completing the physical examination.

Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 2002 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

9.1.4 Statistical Methods

Table 9-1 summarizes the statistical analysis performed for the 2002 general health assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, exclusions, and statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 9-1.

Table 9-1. Statistical Analysis for the General Health Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions	Statistical Analysis and Methods
Self-perception of Health	Q-SR	D	Fair or Poor Excellent or Good	(1)	None	U:LR,CS A:LR
Appearance of Illness or Distress as Assessed by Physician	PE	D	Yes No	(1)	None	U:LR,CS A:LR
Relative Age Appearance as Assessed by Physician	PE	D	Older Same or Younger	(1)	None	U:LR,CS A:LR

Table 9-1. Statistical Analysis for the General Health Assessment

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions	Statistical Analysis and Methods
Body Mass Index (kg/m^2)	PE	C/D	Obese: >30 Not Obese: ≤30	(1)	None	U:LR,CS,GLM,TT A:LR,GLM

[a]Covariates:

(1) age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history, current alcohol use (two weeks prior to physical examination), lifetime alcohol history.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	C/D	Born ≥ 1942 Born < 1942
Race	MIL	D	Black Non-Black
Military Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Current Cigarette Smoking (cigarettes/day)	Q-SR	C/D	Never Former >0–20 >20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	C/D	0 >0–10 >10
Current Alcohol Use (2 weeks prior to physical examination) (drinks/day)	Q-SR	C/D	0–1 >1
Lifetime Alcohol History (drink-years)	Q-SR	C/D	0 >0–40 >40

Abbreviations

Data Source:	MIL: Air Force military records
	PE: 2002 physical examination
	Q-SR: AFHS health questionnaires (self-reported)
Data Form:	D: Discrete form of dependent variable or covariate
	C/D: Continuous and discrete forms of dependent variable; appropriate form for analysis (either continuous or discrete) of covariate
Statistical Analysis:	U: Unadjusted analysis
	A: Adjusted analysis
Statistical Methods:	CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
	GLM: General linear models analysis
	LR: Logistic regression analysis
	TT: Two-sample t-test

Four models were examined for each dependent variable given in Table 9-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for covariates. These covariates are given in Table 9-1. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. In an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-4, the median level of exposure to dioxin was highest for enlisted groundcrew, followed by enlisted flyers, then officers.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the CDC using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in parts per trillion (ppt) on a lipid weight basis (132). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2. A statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model to account for body mass index-related differences in elimination rate (45). This adjustment was accomplished for the unadjusted and adjusted analyses of all dependent variables except body mass index in 2002. The use of body mass index at the time of the participant's blood measurement of dioxin as a covariate may mask the relation between body mass index in 2002 and the dioxin measure.

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. Another category was examined by combining the low and high Ranch Hand categories. This combination is referred to in the tables as the "low plus high Ranch Hand" category. These five categories—Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the four Ranch Hand categories and the dependent variable in the Comparison category was examined. As in Model 2, a statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables except body mass index in 2002. One Ranch Hand without a dioxin measure was excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was

not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The term "unadjusted" was used in the text and tables as follows: Models 1 and 4 did not adjust for any covariates. Models 2 and 3 adjusted only for body mass index at the time of the blood measurement for dioxin, although no such adjustment was made when the dependent variable was body mass index at the time of the 2002 physical examination.

The term "adjusted" was used in the text and tables as follows: Models 1 and 4 adjusted for the covariates shown in Table 9-1 unless otherwise specified by a footnote to the table. Models 2 and 3 additionally adjusted only for body mass index at the time of the blood measurement for dioxin, although no such adjustment was made when the dependent variable was body mass index at the time of the 2002 physical examination.

Table 9-2 provides a summary of the number of participants with missing dependent variable and covariate data.

Table 9-2. Number of Participants with Missing Data for the General Health Assessment

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only) [b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Self-perception of Health	DEP	0	2	0	0	0	2
Appearance of Illness or Distress as Assessed by Physician	DEP	1	0	0	1	1	0
Relative Age Appearance as Assessed by Physician	DEP	1	0	0	1	1	0
Body Mass Index	DEP	1	0	0	1	1	0
Current Cigarette Smoking	COV	0	2	0	0	0	2
Lifetime Cigarette Smoking History	COV	0	3	0	0	0	3
Current Alcohol Use	COV	0	2	0	0	0	2
Lifetime Alcohol History	COV	4	5	3	4	4	5

[a]777 Ranch Hands and 1,174 Comparisons for group.
[b]424 Ranch Hands for initial dioxin; 776 Ranch Hands for 1987 dioxin.
[c]776 Ranch Hands and 1,174 Comparisons for categorized dioxin.

Note: COV = Covariate.
        DEP = Dependent variable.

9.2   RESULTS

9.2.1   Dependent Variable-covariate Associations

The dependent variables in the general health assessment were tested for associations with each of the covariates used in the adjusted analyses. The complete results are presented in Appendix F, Table F-1. These associations were pairwise between the dependent variable and the covariate and were not adjusted

for any other covariates. A brief summary of the pattern of significant (p≤0.05) dependent variable-covariate associations is described in the following paragraphs.

Age was associated with appearance of illness or distress, as well as body mass index in its continuous form. A higher percentage of older participants appeared ill or distressed than the younger participants. Body mass decreased with age.

All dependent variables were associated with military occupation, except for appearance of illness or distress. Enlisted personnel had a higher percentage of abnormal results for self-perception of health and relative age appearance than officers. Officers were classified as obese less often and had a lower mean body mass index than enlisted personnel.

Current cigarette smoking was associated with all dependent variables. The percentage of abnormal results for self-perception of health, appearance of illness or distress, and relative age appearance increased with current cigarette smoking. Body mass decreased as current cigarette smoking levels increased.

Lifetime cigarette smoking was associated with self-perception of health, appearance of illness or distress, and relative age appearance. In each of these dependent variables, the heaviest smokers (in terms of pack-years) had the highest percentage of abnormalities.

Current alcohol use was associated with body mass index in its continuous form. Body mass decreased as current alcohol use increased.

Both self-perception of health and body mass index in its continuous form were associated with lifetime alcohol history. The highest percentage of participants who perceived their health as fair or poor was among nondrinkers, followed by heavy lifetime drinkers and moderate lifetime drinkers. Body mass decreased as lifetime alcohol use increased.

9.2.2   Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 9-1. Dependent variables are grouped into two sections: (1) the questionnaire variable self-perception of health, derived from the questionnaire that was administered in the 2002 follow-up examination, and (2) the physical examination variables, obtained during the 2002 physical examination.

9.2.2.1   Questionnaire Variable

9.2.2.1.1   Self-perception of Health

The unadjusted and adjusted analyses for Models 1 through 4 showed no significant results (Table 9-3(a-d): p>0.05 for each analysis).

Table 9-3. Analysis of Self-perception of Health

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Fair or Poor	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*110 (14.2)*	*1.06 (0.81,1.38)*	*0.672*
	Comparison	*1,172*	*158 (13.5)*		
Officer	Ranch Hand	307	28 (9.1)	1.22 (0.73,2.06)	0.445
	Comparison	462	35 (7.6)		
Enlisted Flyer	Ranch Hand	133	22 (16.5)	0.79 (0.44,1.42)	0.434
	Comparison	185	37 (20.0)		
Enlisted Groundcrew	Ranch Hand	337	60 (17.8)	1.11 (0.77,1.59)	0.587
	Comparison	525	86 (16.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,941*	*1.03 (0.79,1.36)*	*0.822*
Officer	769	1.24 (0.74,2.10)	0.416
Enlisted Flyer	315	0.78 (0.42,1.42)	0.413
Enlisted Groundcrew	857	1.05 (0.72,1.53)	0.805

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Fair or Poor	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	16 (11.4)	1.10 (0.91,1.33)	0.314
Medium	143	34 (23.8)		
High	141	19 (13.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
421	1.16 (0.91,1.47)	0.224

[a]Relative risk for a twofold increase in initial dioxin.

Table 9-3. Analysis of Self-perception of Health (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Fair or Poor	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	158 (13.5)		
Background RH	352	41 (11.6)	0.90 (0.62,1.31)	0.592
Low RH	211	29 (13.7)	1.00 (0.65,1.53)	0.999
High RH	213	40 (18.8)	1.40 (0.95,2.06)	0.085
Low plus High RH	424	69 (16.3)	1.19 (0.87,1.62)	0.285

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	351	1.04 (0.71,1.54)	0.841
Low RH	210	0.97 (0.62,1.51)	0.879
High RH	211	1.12 (0.74,1.69)	0.595
Low plus High RH	421	1.04 (0.75,1.44)	0.817

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Fair or Poor	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	27 (10.4)	1.13 (1.00,1.28)	0.055
Medium	258	34 (13.2)		
High	258	49 (19.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 9-3. Analysis of Self-perception of Health (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
772	1.06 (0.91,1.22)	0.463

[a]Relative risk for a twofold increase in 1987 dioxin.

9.2.2.2   *Physical Examination Variables*

9.2.2.2.1   *Appearance of Illness or Distress as Assessed by Physician*

All unadjusted and adjusted analyses of appearance of illness or distress, as assessed by a physician, were nonsignificant for Models 1 through 4 (Table 9-4(a-h): p>0.10 for each analysis).

Table 9-4. Analysis of Appearance of Illness or Distress

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*776*	*31 (4.0)*	*0.94 (0.59,1.48)*	*0.774*
	Comparison	*1,174*	*50 (4.3)*		
Officer	Ranch Hand	306	12 (3.9)	1.01 (0.48,2.12)	0.986
	Comparison	462	18 (3.9)		
Enlisted Flyer	Ranch Hand	133	11 (8.3)	1.99 (0.78,5.10)	0.150
	Comparison	185	8 (4.3)		
Enlisted Groundcrew	Ranch Hand	337	8 (2.4)	0.51 (0.23,1.15)	0.104
	Comparison	527	24 (4.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,940*	*0.94 (0.58,1.50)*	*0.789*
Officer	768	1.03 (0.48,2.19)	0.946
Enlisted Flyer	315	1.90 (0.72,4.98)	0.193
Enlisted Groundcrew	857	0.52 (0.23,1.21)	0.129

Table 9-4. Analysis of Appearance of Illness or Distress (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a,b]**	**p-Value**
Low	140	5 (3.6)	0.97 (0.67,1.39)	0.862
Medium	143	7 (4.9)		
High	141	5 (3.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
421	1.12 (0.70,1.79)	0.631

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a,b]**	**p-Value**
Comparison	1,174	50 (4.3)		
Background RH	351	14 (4.0)	1.03 (0.56,1.90)	0.916
Low RH	211	10 (4.7)	1.08 (0.53,2.16)	0.839
High RH	213	7 (3.3)	0.70 (0.31,1.57)	0.381
Low plus High RH	424	17 (4.0)	0.86 (0.49,1.53)	0.618

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 9-4. Analysis of Appearance of Illness or Distress (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	350	1.07 (0.57,2.03)	0.827
Low RH	210	0.94 (0.46,1.93)	0.865
High RH	211	0.77 (0.33,1.80)	0.545
Low plus High RH	421	0.85 (0.47,1.54)	0.592

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	8 (3.1)	0.99 (0.79,1.24)	0.928
Medium	258	11 (4.3)		
High	258	12 (4.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
771	1.04 (0.78,1.37)	0.807

[a]Relative risk for a twofold increase in 1987 dioxin.

9.2.2.2.2   Relative Age Appearance as Assessed by Physician

The unadjusted and adjusted analyses in Models 1 and 2 showed no significant results (Table 9-5(a-d): p>0.15 for each analysis).

The unadjusted Model 3 analysis of relative age appearance as assessed by a physician revealed significant differences between Ranch Hands in the high dioxin category and Comparisons (Table 9-5(e): Unadjusted Relative Risk [RR]=2.01, p=0.016), as well as between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 9-5(e): Unadjusted RR=1.73, p=0.023). The

percentages of participants appearing older among Ranch Hands in the high dioxin category, Ranch Hands in the low and high categories combined, and Comparisons were 8.5, 7.3, and 4.1, respectively. After adjusting for covariates, neither difference was significant (Table 9-5(f): p=0.223 for high Ranch Hands versus Comparisons; p=0.116 for low and high Ranch Hands combined).

A significant relation between relative age appearance and 1987 dioxin was seen in the unadjusted Model 4 analysis (Table 9-5(g): Unadjusted RR=1.34, p=0.002). The percentages of Ranch Hands who appeared older than their stated age were 2.3, 4.3, and 9.3 for the low, medium, and high 1987 dioxin categories. After adjusting for covariates, the relation was not significant (p=0.061).

Table 9-5. Analysis of Relative Age Appearance

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Older	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*776*	*42 (5.4)*	*1.34 (0.88,2.05)*	*0.176*
	Comparison	*1,174*	*48 (4.1)*		
Officer	Ranch Hand	306	6 (2.0)	1.30 (0.43,3.91)	0.640
	Comparison	462	7 (1.5)		
Enlisted Flyer	Ranch Hand	133	13 (9.8)	1.07 (0.50,2.29)	0.860
	Comparison	185	17 (9.2)		
Enlisted Groundcrew	Ranch Hand	337	23 (6.8)	1.54 (0.85,2.77)	0.154
	Comparison	527	24 (4.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,940*	*1.28 (0.82,1.98)*	**0.277**
Officer	768	1.33 (0.44,3.99)	0.616
Enlisted Flyer	315	1.05 (0.48,2.29)	0.906
Enlisted Groundcrew	857	1.42 (0.78,2.58)	0.255

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Older	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	6 (4.3)	1.19 (0.92,1.54)	0.194
Medium	143	13 (9.1)		
High	141	12 (8.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 9-5. Analysis of Relative Age Appearance (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
421	1.00 (0.74,1.34)	0.975

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands who appear older than their stated age.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Older	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	48 (4.1)		
Background RH	351	10 (2.8)	0.75 (0.38,1.51)	0.425
Low RH	211	13 (6.2)	1.49 (0.79,2.81)	0.217
High RH	213	18 (8.5)	2.01 (1.14,3.54)	0.016*
Low plus High RH	424	31 (7.3)	1.73 (1.08,2.78)	0.023*

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	350	0.86 (0.42,1.79)	0.695
Low RH	210	1.51 (0.78,2.92)	0.218
High RH	211	1.45 (0.80,2.62)	0.223
Low plus High RH	421	1.48 (0.91,2.41)	0.116

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 9-5. Analysis of Relative Age Appearance (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED				
1987 Dioxin Category Summary Statistics			**Analysis Results for Log$_2$ (1987 Dioxin)**	
1987 Dioxin	**n**	**Number (%) Older**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	259	6 (2.3)	1.34 (1.11,1.62)	0.002**
Medium	258	11 (4.3)		
High	258	24 (9.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
771	1.22 (0.99,1.52)	0.061

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands who appear older than their stated age.

9.2.2.2.3 *Body Mass Index (Continuous)*

No significant associations with dioxin were shown in all Model 1 and 2 unadjusted and adjusted analyses of body mass index in its continuous form (Table 19-6(a-d): p>0.20 for each analysis).

All four contrasts were significant in the unadjusted Model 3 analyses of body mass index (Table 9-6(e): difference of means=-1.20 kg/m^2, p<0.001 for Ranch Hands in the background category versus Comparisons; difference of means=0.81 kg/m^2, p=0.010 for Ranch Hands in the low dioxin category; difference of means=1.20 kg/m^2, p<0.001 for Ranch Hands in the high dioxin category; and difference of means=1.00 kg/m^2, p<0.001 for Ranch Hands in the low and high dioxin categories combined).

Adjusting for covariates revealed similar results (Table 9-6(f): difference of adjusted means=-1.04 kg/m^2, p<0.001 for Ranch Hands in the background category versus Comparisons; difference of adjusted means=0.87 kg/m^2, p=0.006 for Ranch Hands in the low dioxin category; difference of means=1.15 kg/m^2, p<0.001 for Ranch Hands in the high dioxin category; and difference of means=1.01 kg/m^2, p<0.001 for Ranch Hands in the low and high dioxin categories combined).

Both unadjusted and adjusted analyses showed Comparisons had a significantly higher mean body mass index than did Ranch Hands in the background dioxin category (28.85 kg/m^2 versus 27.81 kg/m^2 for the adjusted analysis). Conversely, the adjusted mean body mass index of Ranch Hands in each of the low

(29.72 kg/m^2), high (30.00 kg/m^2), and low and high dioxin categories combined (29.86 kg/m^2) was significantly greater than Comparisons (28.85 kg/m^2).

The Model 4 unadjusted and adjusted analyses each revealed a significant association between 1987 dioxin levels and body mass index (Table 9-6(g): Slope=0.024, p<0.001 and (h): Adjusted Slope=0.026, p<0.001). Body mass index increased as dioxin levels increased. Adjusted mean body mass index values for the low, medium, and high 1987 dioxin categories were 26.93 kg/m^2, 28.88 kg/m^2, and 29.65 kg/m^2, respectively.

Table 9-6. Analysis of Body Mass Index (kg/m^2) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*776*	*28.67*	*-0.03*	*0.880*
	Comparison	*1,174*	*28.70*		
Officer	Ranch Hand	306	28.34	0.06	0.846
	Comparison	462	28.29		
Enlisted Flyer	Ranch Hand	133	28.48	-0.42	0.382
	Comparison	185	28.90		
Enlisted Groundcrew	Ranch Hand	337	29.04	0.05	0.873
	Comparison	527	28.99		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*772*	*28.89*	*0.05*	*0.791*
	Comparison	*1,168*	*28.83*		
Officer	Ranch Hand	306	28.60	0.10	0.737
	Comparison	462	28.50		
Enlisted Flyer	Ranch Hand	132	28.82	-0.24	0.608
	Comparison	183	29.06		
Enlisted Groundcrew	Ranch Hand	334	29.14	0.12	0.695
	Comparison	523	29.03		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 9-6. Analysis of Body Mass Index (kg/m^2) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	140	29.40	0.004	0.007 (0.006)	0.203
Medium	143	29.78			
High	141	29.93			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of body mass index versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	140	29.08	0.106	0.007 (0.006)	0.244
Medium	142	29.47			
High	139	29.49			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of body mass index versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Difference of Unadjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,174	28.70		
Background RH	351	27.50	-1.20	<0.001**
Low RH	211	29.51	0.81	0.010**
High RH	213	29.90	1.20	<0.001**
Low plus High RH	424	29.70	1.00	<0.001**

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 9-6. Analysis of Body Mass Index (kg/m²) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,168	28.85		
Background RH	350	27.81	-1.04	<0.001**
Low RH	210	29.72	0.87	0.006**
High RH	211	30.00	1.15	<0.001**
Low plus High RH	421	29.86	1.01	<0.001**

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log₂ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	259	27.22	0.066	0.024 (0.003)	<0.001**
Medium	258	29.09			
High	258	29.81			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of body mass index versus log₂ (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

Table 9-6. Analysis of Body Mass Index (kg/m^2) (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean**[a]	**R^2**	**Adjusted Slope (Standard Error)**[b]	**p-Value**
Low	259	26.93	0.112	0.026 (0.004)	<0.001**
Medium	257	28.88			
High	255	29.65			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of body mass index versus log$_2$ (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

9.2.2.2.4   *Body Mass Index (Discrete)*

All Model 1 and 2 unadjusted and adjusted analyses of body mass index in its discrete form were nonsignificant (Table 9-7(a-d): p>0.65 for each analysis).

The unadjusted Model 3 analysis of body mass index revealed significant results in all four contrasts (Table 9-7(e): Unadjusted RR=0.55, p<0.001 for Ranch Hands in the background dioxin category; Unadjusted RR=1.44, p=0.016 for the Ranch Hands in the low dioxin category; Unadjusted RR=1.62, p=0.001 for Ranch Hands in the high dioxin category; and Unadjusted RR=1.53, p<0.001 for Ranch Hands in the low and high dioxin categories combined). The percentage of obese participants was higher for Comparisons (35.3%) than for Ranch Hands in the background dioxin category (23.1%). The percentage of obese participants, however, was lower for Comparisons than for Ranch Hands in the low, high, and low and high dioxin categories combined (44.1%, 46.9%, and 45.5%, respectively).

Similarly, all contrasts were significant after adjusting for covariates in Model 3 (Table 9-7(f): Adjusted RR=0.59, p<0.001 for Ranch Hands in the background dioxin category; Adjusted RR=1.48, p=0.011 for the Ranch Hands in the low dioxin category; Adjusted RR=1.52, p=0.009 for Ranch Hands in the high dioxin category; and Adjusted RR=1.50, p=0.001 for Ranch Hands in the low and high dioxin categories combined).

The Model 4 unadjusted and adjusted analyses revealed significant positive associations between body mass index and 1987 dioxin levels (Table 9-7(g): Unadjusted RR=1.31, p<0.001, and (h): Adjusted RR=1.31, p<0.001). The percentages of obese participants in the low, medium, and high 1987 dioxin categories were 21.6, 38.0, and 46.5, respectively.

Table 9-7. Analysis of Body Mass Index (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Obese	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*776*	*274 (35.3)*	*1.00 (0.83,1.21)*	*0.986*
	Comparison	*1,174*	*415 (35.3)*		
Officer	Ranch Hand	306	93 (30.4)	1.01 (0.74,1.39)	0.928
	Comparison	462	139 (30.1)		
Enlisted Flyer	Ranch Hand	133	48 (36.1)	0.97 (0.61,1.54)	0.903
	Comparison	185	68 (36.8)		
Enlisted Groundcrew	Ranch Hand	337	133 (39.5)	1.00 (0.76,1.32)	0.999
	Comparison	527	208 (39.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,940*	*1.02 (0.84,1.24)*	*0.827*
Officer	768	1.03 (0.75,1.41)	0.873
Enlisted Flyer	315	1.01 (0.63,1.62)	0.976
Enlisted Groundcrew	857	1.02 (0.77,1.36)	0.874

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Obese	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	140	64 (45.7)	1.03 (0.90,1.19)	0.653
Medium	143	64 (44.8)		
High	141	65 (46.1)		

[a]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
421	1.03 (0.86,1.23)	0.744

[a]Relative risk for a twofold increase in initial dioxin.

Table 9-7. Analysis of Body Mass Index (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Obese	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,174	415 (35.3)		
Background RH	351	81 (23.1)	0.55 (0.42,0.72)	<0.001**
Low RH	211	93 (44.1)	1.44 (1.07,1.94)	0.016*
High RH	213	100 (46.9)	1.62 (1.21,2.17)	0.001**
Low plus High RH	424	193 (45.5)	1.53 (1.22,1.91)	<0.001**

[a]Relative risk and confidence interval relative to Comparisons.

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	350	0.59 (0.45,0.79)	<0.001**
Low RH	210	1.48 (1.09,2.01)	0.011*
High RH	211	1.52 (1.11,2.07)	0.009**
Low plus High RH	421	1.50 (1.19,1.89)	0.001**

[a]Relative risk and confidence interval relative to Comparisons.

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 9-7. Analysis of Body Mass Index (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Obese	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	56 (21.6)	1.31 (1.19,1.44)	<0.001**
Medium	258	98 (38.0)		
High	258	120 (46.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
771	1.31 (1.17,1.47)	<0.001**

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

9.3   DISCUSSION

The following four factors were considered when assessing the overall state of participant health in the 2002 AFHS: self-perception of health, appearance of illness, relative age, and body mass index. Clinicians often employ such measures to assess an overall state of health rather than a specific organ system. While these measures may be imperfect and were no doubt influenced by many variables, they do reflect overall health impressions from both self and observer perspectives.

The covariates included in the analysis were age, race, military occupation, current and lifetime cigarette smoking, and current and lifetime alcohol consumption. Such covariates gave insight into the factors having the most impact on general health measurements and helped to clarify whether findings of associations with herbicides or measures of dioxin were due to dioxin exposure or to factors that may not have been matched between groups in the design of the AFHS.

The relation between covariates and the general health endpoints were consistent with findings that are well established in clinical practice. Older participants were more likely to appear ill than younger participants. Analysis of body mass index also showed that age was inversely associated with body mass index. This result was consistent with other studies showing that adults older than 55 tend to lose weight (133).

Officers more often perceived their health to be in the "excellent" or "good" categories than did enlisted personnel. Many factors could have contributed to this observed association, such as the various levels of

education among the groups. Some studies have revealed that a higher level of formal education has a major impact on health status and the outcomes of most chronic diseases (134). Enlisted flyers appeared older than officers or enlisted groundcrew.

The association of smoking with ill appearance in this study underscores the pervasive effects of smoking on health. Both lifetime and current cigarette smoking were significantly associated with the perception of overall health, appearance of illness, and relative age appearance. In all cases, the more cigarettes smoked, the greater the likelihood the participants perceived themselves as ill or appeared ill. These results concur with the vast amount of literature that implicates smoking exposure as a major risk to overall health (135).

Former smokers perceived a level of health that approximates the "never smoker" level. This effect was consistent with other studies showing that some of the deleterious effects of smoking are reversible, such as the improvement of bronchial dysfunction commonly associated with active smoke exposure (136).

Current smoking also was associated with a decrease in body mass index. As the amount of cigarettes smoked increases, the percentage of obese participants decreased. This result was consistent with the common association made between smoking and weight loss.

General health, as measured in terms of self-perception, showed no significant differences in the studied populations by herbicide or dioxin exposure. Although some participants know their exposure levels and may have had concerns, such information did not appear to have had a significant effect on their perceived overall health at the 2002 follow-up examination.

During the course of the AFHS, however, self-perception of general health has shown mixed results since 1982. For example, the 1982 baseline study indicated that a greater percentage of Ranch Hands than Comparisons reported fair or poor health (20.6% for Ranch Hands versus 14.2% for Comparisons), as did the 1992 and 1997 follow-up examinations (10.4% of Ranch Hands versus 7.4% of Comparisons and 14.3% versus 10.4%, respectively). But in the 1985, 1987, and 2002 studies, no appreciable differences were seen between Ranch Hands and Comparisons. Thus, no persistent or emergent impact of herbicide or dioxin exposure on this general health measure has been observed, raising the possibility that participant concern regarding exposure decreased over time.

In 2002, the appearance of illness or distress as assessed by the examining physicians disclosed no differences between the Ranch Hand and Comparison groups, a finding similar to results reported in previous AFHS examinations. The appearance of illness classification was reserved for a relatively low percentage (approximately 4%) of participants who had significant manifestations of illness, such as cachexia and frailty.

The Ranch Hand and Comparison groups did not show any significant differences in appearing older than expected. Likewise, analysis did not suggest any association between appearing older than expected and dioxin levels. These results were generally consistent with previous AFHS results that showed no association between herbicide or dioxin exposure and relative age appearance.

The body mass index, a measurement of relative weight that adjusts for height, serves as a valuable clinical clue to the presence of disease and helps define obesity—an important health risk factor. Contrasts on body mass index showed no statistically significant difference between the Ranch Hand and Comparison groups or in initial dioxin levels within the Ranch Hands; however, in the categorized dioxin analyses, there was a detectable increase in the mean body mass index compared to the Comparison group for the low and high Ranch Hand dioxin categories. Likewise, 1987 dioxin levels were associated with

increased obesity in the analyses. Increased percentages of obesity were observed in relation to increasing dioxin exposure.

The 2002 body mass index results were similar to previous AFHS follow-up examinations in that obesity was highly correlated with dioxin levels. This association appears to be due to slower dioxin elimination pharmacokinetics in obese participants relative to participants who were lean or not obese. In part, participants with the highest dioxin levels retain dioxin due to their higher body fat content. A remarkable finding was that the prevalence of obesity in the participant population approaches 35 percent, which was somewhat greater than the national average of approximately 30 percent (137). Therefore, more than one-third of AFHS participants are at risk for health complications associated with obesity.

9.4 SUMMARY

The general health assessment was based on perception of health, as reported in the questionnaire by the participant, and physical examination data. Associations with herbicide exposure (i.e., group – Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable in the general health assessment. The significant adjusted results are discussed in the sections below.

9.4.1 Model 1: Group Analysis

All group analyses (Ranch Hands versus Comparisons) revealed no significant differences between Ranch Hands and Comparisons overall or within each occupation. The results are summarized in Table 9-8.

Table 9-8. Summary of Group Analysis (Model 1) for General Health Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Questionnaire				
Self-perception of Health (D)	NS	NS	ns	NS
Physical Examination				
Appearance of Illness or Distress (D)	ns	NS	NS	ns
Relative Age Appearance (D)	NS	NS	NS	NS
Body Mass Index (C)	ns	NS	ns	NS
Body Mass Index (D)	NS	NS	ns	NS

Note: NS or ns: Not significant (p>0.05).
  C: Continuous form of dependent variable.
  D: Discrete form of dependent variable.

  A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

	ADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Questionnaire				
Self-perception of Health (D)	NS	NS	ns	NS
Physical Examination				
Appearance of Illness or Distress (D)	ns	NS	NS	ns
Relative Age Appearance (D)	NS	NS	NS	NS
Body Mass Index (C)	NS	NS	ns	NS
Body Mass Index (D)	NS	NS	NS	NS

Note: NS or ns: Not significant ($p > 0.05$).
    C: Continuous form of dependent variable.
    D: Discrete form of dependent variable.

    A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

9.4.2   Model 2: Initial Dioxin Analysis

Each variable examined in the analyses of initial dioxin showed no significant findings. Results are displayed in Table 9-9.

Table 9-9. Summary of Initial Dioxin Analysis (Model 2) for General Health Variables (Ranch Hands Only)

Variable	**Unadjusted**	**Adjusted**
Questionnaire		
Self-perception of Health (D)	NS	NS
Physical Examination		
Appearance of Illness or Distress (D)	ns	NS
Relative Age Appearance (D)	NS	NS
Body Mass Index (C)	NS	NS
Body Mass Index (D)	NS	NS

Note: NS or ns: Not significant ($p > 0.05$).
    C: Continuous form of dependent variable.
    D: Discrete form of dependent variable.

    A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

9.4.3   Model 3: Categorized Dioxin Analysis

Table 9-10 summarizes the results of the categorized dioxin analyses. The analyses of categorized dioxin yielded similar results for body mass index in its continuous form. The mean body mass index in the background Ranch Hand category was significantly lower than the Comparison mean, and the means in the low, high, and low and high combined Ranch Hand dioxin categories were significantly higher than the Comparison mean.

Analyses of body mass index in its discrete form revealed a significantly lower percentage of obese Ranch Hands in the background dioxin category, and a significantly higher percentage of obese Ranch Hands in the low, high, and low and high Ranch Hand categories combined, than Comparisons.

Table 9-10. Summary of Categorized Dioxin Analysis (Model 3) for General Health Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Questionnaire				
Self-perception of Health (D)	ns	NS	NS	NS
Physical Examination				
Appearance of Illness or Distress (D)	NS	NS	ns	ns
Relative Age Appearance (D)	ns	NS	p=0.016 (2.01)	p=0.023 (1.73)
Body Mass Index (C)	p<0.001 (-1.20)	p=0.010 (0.81)	p<0.001 (1.20)	p<0.001 (1.00)
Body Mass Index (D)	p<0.001 (0.55)	p=0.016 (1.44)	p=0.001 (1.62)	p<0.001 (1.53)

Note: NS or ns: Not significant ($p>0.05$).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

      The p-value was given if $p\leq0.05$. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

      A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Questionnaire				
Self-perception of Health (D)	NS	ns	NS	NS
Physical Examination				
Appearance of Illness or Distress (D)	NS	ns	ns	ns
Relative Age Appearance (D)	ns	NS	NS	NS
Body Mass Index (C)	p<0.001 (-1.04)	p=0.006 (0.87)	p<0.001 (1.15)	p<0.001 (1.01)
Body Mass Index (D)	p<0.001 (0.59)	p=0.011 (1.48)	p=0.009 (1.52)	p=0.001 (1.50)

Note: NS or ns: Not significant (p>0.05).
   C: Continuous form of dependent variable.
   D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

9.4.4   Model 4: 1987 Dioxin Level Analysis

The associations between the measures of general health studied in this assessment and the 1987 dioxin levels are presented in Table 9-11. The adjusted analysis showed that body mass index in both the continuous and discrete forms was significant.

Table 9-11. Summary of 1987 Dioxin Analysis (Model 4) for General Health Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Questionnaire		
Self-perception of Health (D)	NS	NS
Physical Examination		
Appearance of Illness or Distress (D)	ns	NS
Relative Age Appearance (D)	p=0.002 (1.34)	NS
Body Mass Index (C)	p<0.001 (0.024)	p<0.001 (0.026)
Body Mass Index (D)	p<0.001 (1.31)	p<0.001 (1.31)

Note: NS or ns: Not significant (p>0.05).
   C: Continuous form of dependent variable.
   D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

9.4.5   Summary of Significant Results

Table 9-12 summarizes the significant results (p≤0.05) for the adjusted analyses that were performed for the general health assessment. The dependent variable and its table reference are listed along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics

that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and is explained in footnotes.

Table 9-12. Summary of Results from Significant Adjusted Analyses in the General Health Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Body Mass Index (9-6)	3	Background RH vs. C	<0.001	-1.04	RH: 27.81 kg/m^2 C: 28.85 kg/m^2	(a)
	3	Low RH vs. C	0.006	0.87	RH: 29.72 kg/m^2 C: 28.85 kg/m^2	(a)
	3	High RH vs. C	<0.001	1.15	RH: 30.00 kg/m^2 C: 28.85 kg/m^2	(a)
	3	Low plus High RH vs. C	<0.001	1.01	RH: 29.86 kg/m^2 C: 28.85 kg/m^2	(a)
	4	All RH: 1987 dioxin	<0.001	0.026 (0.004)	Low: 26.93 kg/m^2 Medium: 28.88 kg/m^2 High: 29.65 kg/m^2	(b)
Body Mass Index (9-7)	3	Background RH vs. C	<0.001	0.59 (0.45,0.79)	RH: 23.1% C: 35.3%	(c)
	3	Low RH vs. C	0.011	1.48 (1.09,2.01)	RH: 44.1% C: 35.3%	(c)
	3	High RH vs. C	0.009	1.52 (1.11,2.07)	RH: 46.9% C: 35.3%	(c)
	3	Low plus High RH vs. C	0.001	1.50 (1.19,1.89)	RH: 45.5% C: 35.3%	(c)
	4	All RH: 1987 Dioxin	<0.001	1.31 (1.17,1.47)	Low: 21.6% Medium: 38.0% High: 46.5%	(d)

(a): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was performed on natural logarithm scale; adjusted means were transformed to original scale and were presented for each dioxin category in contrast.

(b): Continuous variable: slope and standard error were presented and were based on natural logarithm of dependent variable versus $\log_2$ (1987 dioxin); adjusted means were transformed to original scale and were presented for each of three 1987 dioxin categories.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

Note: RH = Ranch Hand.
        C = Comparison.

Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
           Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
           High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Model 4:   Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

9.5   CONCLUSION

Self-perception of health, appearance of illness, and relative age appearance were not found to be associated with herbicide exposure (Ranch Hand versus Comparison) or dioxin level. Body mass index was positively associated with 1987 dioxin, possibly reflecting the pharmacokinetics of dioxin elimination.

REFERENCES

1. Rao, V.R. 1991. Molecular mechanism of action of dioxin-implications of its carcinogenic potency estimation. *Toxic Substances Journal* 8:335-51.

2. Huff, J., G. Lucier, and A. Tritscher. 1994. Carcinogenicity of TCDD: Experimental, mechanistic, and epidemiologic evidence. *Annual Review of Pharmacology and Toxicology* 34:343-72.

3. Neubert, D. 1992. Evaluation of toxicity of TCDD in animals as a basis for human risk assessment. *Toxic Substances Journal* 12:237-76.

4. Birnbaum, L.S. 1993. EPA's reassessment of dioxin risk: Directed health research. *Chemosphere* 27:469-75.

5. Dickson, L.C., and S.C. Buzik. 1993. Health risks of "dioxins": A review of environmental and toxicological considerations. *Veterinary and Human Toxicology* 35(1):68-77.

6. Houk, V.N. 1992. Review of research on health effects of PCDDs and PCDFs to develop human risk assessment. *Toxic Substances Journal* 12:181-90.

7. Kakeyama, M., and C. Tohyama. 2003. Developmental neurotoxicity of dioxin and its related compounds. *Industrial Health* 41:215-30.

8. Yonemoto, J. 2000. The effects of dioxin on reproduction and development. *Industrial Health* 38:259-68.

9. Poland, A., and J.C. Knutson. 1982. 2,3,7,8-tetrachlorodibenzo-p-dioxin and related halogenated aromatic hydrocarbons: Examination of the mechanism of toxicity. *Annual Review of Pharmacology and Toxicology* 22:517-54.

10. Denison, M.S. 1992. Heterogeneity of rat hepatic Ah receptor: Identification of two receptor forms which differ in their biochemical properties. *Journal of Biochemical Toxicology* 7(4)249-56.

11. Denison, M.S., L.M. Vella, and A.B. Okey. 1986. Structure and function of the Ah receptor for 2,3,7,8-tetrachlorodibenzo-p-dioxin. Species difference in molecular properties of the receptors from mouse and rat hepatic cytosols. *Journal of Biological Chemistry* 261(9):3987-95.

12. Okey, A.B., D.S. Riddick, and P.A. Harper. 1994. The Ah receptor: Mediator of the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. *Toxicology Letters* 70(1):1-22.

13. Roberts, E.A., K.C. Johnson, P.A. Harper, and A.B. Oakley. 1990. Characterization of the Ah receptor mediating aryl hydrocarbon hydroxylase induction in the human liver cell line Hep G2. *Archives of Biochemistry and Biophysics* 276(2):442-50.

14. Waithe, W.I., M. Michaud, P.A. Harper, A.B. Okey, and A. Anderson. 1991. The Ah receptor, cytochrome P450IA1 mRNA induction, and aryl hydrocarbon hydroxylase in a human lymphoblastoid cell line. *Biochemical Pharmacology* 41(1):85-92.

15. Lorenzen, A., and A.B. Okey. 1991. Detection and characterization of Ah receptor in tissue and cells from human tonsils. *Toxicology and Applied Pharmacology* 107(2):203-14.

16. Lucier, G. 1991. Humans are sensitive species to some of the biochemical effects of structural analogs of dioxin. *Environmental Toxicology and Chemistry* 10:727-35.

17. Mimura, J., and Y. Fujii-Kuriyama. 2003. Functional role of AhR in the expression of toxic effects by TCDD. *Biochimica et Biophysica Acta* 1619:263-68.

18. Wang, X., R. Rosengren, V. Morrison, and S. Safe. 1992. Characterization of the human Ah receptor. *Chemosphere* 25:997-1000.

19. Wang, X., M. Santostefano, Y. Lu, and S. Safe. 1992. A comparison of the mouse versus human aryl hydrocarbon (Ah) receptor complex: Effects of proteolysis. *Chemico-Biological Interactions* 85(1):79-93.

20. Institute of Medicine. 2003. Veterans and Agent Orange: Update 2002. National Academy Press: Washington, DC.

21. Kancir, C.B., C. Andersen, and A.S. Olesen. 1988. Marked hypocalcemia in a fatal poisoning with chlorinated phenoxy acid derivatives. *Clinical Toxicology* 23(3-4):257-64.

22. Flanagan, R.J., T.J. Meredith, M. Ruprah, L.J. Onyon, and A. Liddle. 1990. Alkaline diuresis for acute poisoning with chlorophenoxy herbicides and ioxynil. *Lancet* 335(8687):454-8.

23. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline morbidity study results. NTIS: AD A 138 340. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

24. Lathrop, G.D., S.G. Machado, T.G. Karrison, W.D. Grubbs, W.F. Thomas, W.H. Wolfe, J.E. Michalek, J.C. Miner, and M.R. Peterson. 1987. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188 262. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

25. Thomas, W.F., W.D. Grubbs, T.G. Karrison, M.B. Lustik, R.H. Roegner, D.E. Williams, W.H. Wolfe, J.E. Michalek, J.C. Miner, and R.W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

26. Roegner, R.H., W.D. Grubbs, M.B. Lustik, A.S. Brockman, S.C. Henderson, D.E. Williams, W.H. Wolfe, J.E. Michalek, and J.C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

27. Grubbs, W.D., W.H. Wolfe, J.E. Michalek, D.E. Williams, M.B. Lustik, A.S. Brockman, S.C. Henderson, F.R. Burnett, R.G. Land, D.J. Osborne, V.K. Rocconi, M.E. Schreiber, J.C. Miner, G.L. Henriksen, and J.A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1992 followup examination results. NTIS: AD A 304 306, 304 308-316. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

28. Visintainer, P.F., M. Barone, H. McGee, and E.L. Peterson. 1995. Proportionate mortality study of Vietnam-era veterans of Michigan. *Journal of Occupational and Environmental Medicine* 37(4):423-8.

29. U.S. Centers for Disease Control (Vietnam Experience Study). 1989. Health status of Vietnam veterans. U.S. Dept. of Health and Human Services Public Health Service Centers for Disease Control Center for Environmental Health and Injury Control: Atlanta, GA.

30. Selected Cancers Cooperative Study Group and Center for Environmental Health and Injury Control (Agent Orange Projects). 1990. The association of selected cancers with service in the U.S. military in Vietnam: Final report. U.S. Department of Health and Human Services Public Health

Service Centers for Disease Control Center for Environmental Health and Injury Control Agent Orange Projects: Atlanta, GA.

31. Dalager, N.A., H.K. Kang, and T.L. Thomas. 1995. Cancer mortality patterns among women who served in the military: The Vietnam experience. *Journal of Occupational and Environmental Medicine* 37:298-305.

32. Bullman, T.A., K.K. Watanabe, and H.K. Kang. 1994. Risk of testicular cancer associated with surrogate measures of Agent Orange exposure among Vietnam veterans on the Agent Orange Registry. *Annals of Epidemiology* 4(1):11-6.

33. Wolfe, W.H., J.E. Michalek, J.C. Miner, A. Rahe, J. Silva, W.F. Thomas, W.D. Grubbs, M.B. Lustik, T.G. Karrison, R.H. Roegner, and D.E. Williams. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. I. Physical health. *The Journal of the American Medical Association* 264:1824-31.

34. Michalek, J.E., B.R. Burnham, H.E. Marden, Jr., J.N. Robinson, V.V. Elequin, J.C. Miner, R.W. Ogershok, W.K. Sneddon, W.D. Grubbs, B.C. Cooper, R.G. Land, V.K. Rocconi, M.E. Yeager, D.E. Williams, and M.E.B. Owens. 2000. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1997 follow-up examination results. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

35. Barrett, D.H., R.D. Morris, F.Z. Akhtar, and J.E. Michalek. 2001. Serum dioxin and cognitive functioning among veterans of Operation Ranch Hand. *Neurotoxicology* 22(4):491-502.

36. Michalek, J.E, F.Z. Akhtar, J.C. Arezzo, D. Garabrant, and J.W. Albers. 2001. Serum dioxin and peripheral neuropathy in veterans of Operation Ranch Hand. *Neurotoxicology* 22(4):479-90.

37. Michalek, J.E., F.Z. Akhtar, and J.L. Kiel. 1999. Serum dioxin, insulin, fasting glucose, and sex hormone-binding globulin in veterans of Operation Ranch Hand. *Journal of Clinical Endocrinology and Metabolism* 84(5):1540-3.

38. Michalek, J.E., F.Z. Akhtar, M.P. Longnecker, and J.E. Burton. 2001. Relation of serum 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) level to hematological examination results in veterans of Operation Ranch Hand. *Archives of Environmental Health* 56(5):396-405.

39. Michalek, J.E., D.H. Barrett, R.D. Morris, and W.G. Jackson, Jr. 2003. Serum dioxin and psychological functioning in U.S. Air Force veterans of the Vietnam War. *Military Medicine* 168(2):153-9.

40. Michalek, J.E., N.S. Ketchum, and F.Z. Akhtar. 1998. Postservice mortality of US Air Force veterans occupationally exposed to herbicides in Vietnam: 15-year follow-up. *American Journal of Epidemiology* 148(8):786-92.

41. Michalek, J.E., N.S. Ketchum, and I.J. Check. 1999. Serum dioxin and immunologic response in veterans of Operation Ranch Hand. *American Journal of Epidemiology* 149(11):1038-46.

42. Michalek, J.E., N.S. Ketchum, and M.P. Longnecker. 2001. Serum dioxin and hepatic abnormalities in veterans of Operation Ranch Hand. *Annals of Epidemiology* 11(5):304-11.

43. Michalek, J.E., N.S. Ketchum, and R.C. Tripathi. 2003. Diabetes mellitus and 2,3,7,8-tetrachlorodibenzo-p-dioxin elimination in veterans of Operation Ranch Hand. *Journal of Toxicology and Environmental Health* 66(3):211-21.

44. Michalek, J.E., J.L. Pirkle, L.L. Needham, D.G. Patterson, Jr., S.P. Caudill, R.C. Tripathi, and P. Mocarelli. 2002. Pharmacokinetics of 2,3,7,8-tetrachlorodibenzo-p-dioxin in Seseso adults and

veterans of operation Ranch Hand. *Journal of Exposure Analysis and Environmental Epidemiology* 12(1):44-53.

45. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57(6):369-78.

46. Kim, H.A, E.M. Kim, Y.C. Park, J.Y. Yu, S.K. Hong, S.H. Jeon, K.L. Park, S.J. Hur, and Y. Heo. 2003. Immunotoxicological effects of Agent Orange exposure to the Vietnam War Korean veterans. *Industrial Health* 41:158-66.

47. Kim, J.S., H.S Lim, S.I. Cho, H.K. Cheong, and M.K. Lim. 2003. Impact of Agent Orange exposure among Korean Vietnam veterans. *Industrial Health* 41:149-57.

48. Asp, S., V. Riihimaki, S. Hernberg, and E. Pukkala. 1994. Mortality and cancer morbidity of Finnish chlorophenoxy herbicide applicators: An 18-year prospective follow-up. *American Journal of Industrial Medicine* 26(2):243-53.

49. Fingerhut, M.A., W.E. Halperin, D.A. Marlow, L.A. Piacitelli, P.A. Honchar, M.H. Sweeney, A.L. Greife, P.A. Dill, K. Steenland, and A. J. Suruda. 1991. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324(4):212-8.

50. Bueno de Mesquita, H.B., G. Doornbos, D.A. Van der Kuip, M. Kogevinas, and R. Winkelmann. 1993. Occupational exposure to phenoxy herbicides and chlorophenols and cancer mortality in the Netherlands. *American Journal of Industrial Medicine* 23(2):289-300.

51. Saracci, R., M. Kogenvinas, P.A. Bertazzi, B.H. Bueno de Mesquita, D. Coggon, L.M. Green, T. Kauppinen, K.A. L'Abbe, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, J. Osman, N. Pearce, and R. Winkelmann. 1991. Cancer mortality in workers exposed to chlorophenoxy herbicides and chlorophenols. *Lancet* 38(8774):1027-32.

52. Coggon, D., B. Pannett, and P. Winter. 1991. Mortality and incidence of cancer at four factories making phenoxy herbicides. *British Journal of Industrial Medicine* 48(3):173-8.

53. Eriksson, M., and L. Hardell. 1991. New experiences strengthen the connection between dioxins, phenoxy acids and malignant tumors. *Lakartidningen* 88(24):2210-1.

54. Eriksson, M., L. Hardell, H. Malker, and J. Weiner. 1992. Malignant lymphoproliferative diseases in occupations with potential exposure to phenoxyacetic acid or dioxins: A register-based study. *American Journal of Industrial Medicine* 22(3):305-12.

55. Manz, A., J. Berger, J.H. Dwyer, D. Flesch-Janys, S. Nagel, and H. Waltsgott. 1991. Cancer mortality among workers in chemical plant contaminated with dioxin. *Lancet* 338(8773):959-64.

56. Eriksson, M., L. Hardell, and H.O. Adami. 1990. Exposure to dioxins as a risk factor for soft tissue sarcoma: A population-based case-control study. *Journal of the National Cancer Institute* 82(6):486-90.

57. Kogevinas, M., R. Saracci, P.A. Bertazzi, B.H. Bueno de Mesquita, D. Coggon, L.M. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, J. Osman, N. Pearce, and R. Winkelmann. 1992. Cancer mortality from soft-tissue sarcoma and malignant lymphomas in an international cohort of workers exposed to chlorophenoxy herbicides and chlorophenols. *Chemosphere* 25:1071-6.

58. Kogevinas, M., T. Kauppinen, R. Winkelmann, H. Becher, P.A. Bertazzi, B. Bas, D. Coggon, D. Green, E. Johnson, M. Littorin, E. Lynge, D.A. Marlow, J.D. Mathews, M. Neuberger, T. Benn, B. Pannett, N. Pearce, and R. Saracci. 1995. Soft tissue sarcoma and non-Hodgkin's lymphoma in workers exposed to phenoxy herbicides, chlorophenols and dioxins: Two nested case-control studies. *Epidemiology* 6(4):396-402.

59. Hardell, L., M. Eriksson, and A. Degerman. 1994. Exposure to phenoxyacetic acids, chlorophenols, or organic solvents in relation to histopathology, stage, and anatomical localization of non-Hodgkin's lymphoma. *Cancer Research* 54(9):2386-9.

60. Calvert, G.M., M.H. Sweeney, M.A. Fingerhut, R.W. Hornung, and W.E. Halperin. 1994. Evaluation of porphyria cutanea tarda in U.S. workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *American Journal of Industrial Medicine* 25(4):559-71.

61. Pelclová, D., Z. Fenclová, J. Preiss, B. Procházka, J. Spácil, Z. Dubská, B. Okrouhlík, E. Lukás, and P. Urban. 2002. Lipid metabolism and neuropsychological follow-up study of workers exposed to 2,3,7,8- tetrachlorodibenzo-p-dioxin. *International Archives of Occupational and Environmental Health* 75(Suppl 1):60-6.

62. Steenland, K., J. Deddens, and L. Piacitelli. 2001. Risk assessment for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) based on an epidemiologic study. *American Journal of Epidemiology* 154(5):451-8.

63. Pelclová, D., Z. Fenclová, Z. Dlaskova, P. Urban, E. Lukás, B. Procházka, C. Rappe, J. Preiss, A. Kocan, and J. Vejlupkova. 2001. Biochemical, neuropsychological, and neurological abnormalities following 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure. *Archives of Environmental Health* 56(6):493-500.

64. Neuberger, M., C. Rappe, S. Bergek, H. Cai, M. Hansson, R. Jager, M. Kundi, C.K. Lim, H. Wingfors, and A.G. Smith. 1999. Persistent health effects of dioxin contamination in herbicide production. *Environmental Research* 81(3):206-14.

65. Ott, M.G., and A. Zober. 1996. Cause specific mortality and cancer incidence among employees exposed to 2,3,7,8-TCDD after a 1953 reactor accident. *Occupational and Environmental Medicine* 53(9):606-12.

66. Ott, M.G., and A. Zober. 1996. Morbidity study of extruder personnel with potential exposure to brominated dioxins and furans. II. Results of clinical laboratory studies. *Occupational and Environmental Medicine* 53(12):844-6.

67. D. Flesch-Janys, H. Becher, P. Gurn, D. Jung, J. Konietzko, A. Manz, and O. Papke. 1996. Elimination of polychlorinated dibenzo-p-dioxins and dibenzofurans in occupationally exposed persons. *Journal of Toxicology and Environmental Health* 47(4):363-78.

68. Zober, A., M.G. Ott, and P. Messerer. 1994. Morbidity follow up study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51(7):479-86.

69. Van der Molen, G.W., B.A. Kooijman, J. Wittsiepe, P. Schrey, D. Flesch-Janys, and W. Slob. 2000. Estimation of dioxin and furan elimination rates with a pharmacokinetic model. *Journal of Exposure Analysis and Environmental Epidemiology* 19(6 Pt. 1):579-85.

70. Ernst, M., D. Flesch-Janys, I. Morgenstern, and A. Manz. 1998. Immune cell functions in industrial workers after exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin: Dissociation of antigen-specific T-cell responses in cultures of diluted whole blood and of isolated peripheral blood mononuclear cells. *Environmental Health Perspectives* 106(Suppl 2):701-5.

71. Jung, D., P.A. Berg, L. Edler, W. Ehrenthal, D. Fenner, D. Flesch-Janys, C. Huber, R. Klein, C. Koitka, G. Lucier, A. Manz, A. Muttray, L. Needham, O. Päpke, M. Pietsch, C. Portier, D. Patterson, W. Prellwitz, D.M. Rose, A. Thews, and J. Konietzko. 1998. Immunologic findings in workers formerly exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin and its congeners. *Environmental Health Perspectives* 106(Suppl 2):689-95.

72. Becher, H., K. Steindorf, and D. Flesch-Janys. 1998. Quantitative cancer risk assessment for dioxins using an occupational cohort. *Environmental Health Perspectives* 106(Suppl 2):663-70.

73. Flesch-Janys, D., K. Steindorf, P. Gurn, and H. Becher. 1998. Estimation of the cumulated exposure to polychlorinated dibenzo-p-dioxins/furans and standardized mortality ratio analysis of cancer mortality by dose in an occupationally exposed cohort. *Environmental Health Perspectives* 106(Suppl 2):655-62.

74. Vena, J., P. Boffetta, H. Becher, T. Benn, H. Bas Bueno-de-Mesquita, D. Coggon, D. Colin, D. Flesch-Janys, L. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, N. Pearce, A.C. Pesatori, R. Saracci, K. Steenland, and M. Kogevinas. 1998. Exposure to dioxin and nonneoplastic mortality in the expanded IARC international cohort study of phenoxy herbicide and chlorophenol production workers and sprayers. *Environmental Health Perspectives* 106(Suppl 2):645-53.

75. Becher, H., and D. Flesch-Janys. 1998. Dioxins and furans: Epidemiologic assessment of cancer risks and other human health effects. *Environmental Health Perspectives* 106(Suppl 2):623-4.

76. Ryan, J.J., and A. Schecter. 2000. Exposure of Russian phenoxy herbicide producers to dioxins. *Journal of Occupational and Environmental Medicine* 42:861-70.

77. Steenland, K., and J. Deddens. 2003. Dioxin: Exposure-response analyses and risk assessment. *Industrial Health* 41:175-80.

78. Kumagai, S., S. Koda, and H. Oda. 2003. Exposure evaluation of dioxins in municipal waste incinerator workers. *Industrial Health* 41:167-74.

79. Takata, T. 2003. Survey on the health effects of chronic exposure to dioxins and its accumulation on workers of a municipal solid waste incinerator, rural part of Osaka Prefecture, and the results of extended survey afterwards. *Industrial Health* 41:189-96.

80. Collins, J.J., M.E. Strauss, G.J. Levinskas, and P.R. Conner. 1993. The mortality experience of workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin in a trichlorophenol-process accident. *Epidemiology* 4(1):7-13.

81. Assennato, G., D. Cervino, E.A. Emmett, G. Longo, and F. Merlo. 1989. Followup of subjects who developed chloracne following TCDD exposure at Seveso. *American Journal of Industrial Medicine* 16(2):119-25.

82. Assennato, G., P. Cannatelli, E. Emmett, I. Ghezzi, and F. Merlo. 1989. Medical monitoring of dioxin clean-up workers. *American Industrial Hygiene Association Journal* 50(11):586-92.

83. Bertazzi, P. 1991. Long-term effects of chemical disasters. Lessons and results from Seveso. *Science of the Total Environment* 106(1-2):5-20.

84. Bertazzi, P. A., A. C. Pesatori, D. Consonni, A. Tironi, M. T. Landi, and C. Zocchetti. 1993. Cancer incidence in a population accidentally exposed to 2,3,7,8-tetrachlorodibenzo-para-dioxin. *Epidemiology* 4(5):398-406.

85. Mocarelli, P., A. Marocchi, P. Brambilla, P. Gerthoux, L. Colombo, A. Mondonico, and L. Meazza. 1991. Effects of dioxin exposure in humans at Seveso, Italy. In: Banbury Report 35: Biological Basis for Risk Assessment of Dioxins and Related Compounds. M.A. Gallo, R.J. Scheuplein, and K.A. van der Heijden, eds. Cold Spring Harbor Laboratory Press: Plainview, NY.

86. Zober, A., P. Messerer, and P. Huber. 1990. Thirty-four-year mortality followup of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. *International Archives of Occupational and Environmental Health* 62(2):139-57.

87. Zober, M. A., M. G. Ott, O. Papke, K. Senft, and C. Germann. 1992. Morbidity study of extruder personnel with potential exposure to brominated dioxins and furans. I. Results of blood monitoring and immunological tests. *British Journal of Industrial Medicine* 49(8):532-44.

88. Sweeney, M.H., and P. Mocarelli. 2000. Human health effects after exposure to 2,3,7,8-TCDD. *Food Additives and Contaminants* 17(4):303-16.

89. Pesatori, A.C., D. Consonni, S. Bachetti, C. Zocchetti, M. Bonzini, A. Baccarelli, and P.A. Bertazzi. 2003. Short- and long-term morbidity and mortality in the population exposed to dioxin after the "Seveso Accident." *Industrial Health* 41:127-38.

90. Landi, M.T, P.A. Bertazzi, A. Baccarelli, D. Consonni, S. Masten, G. Lucier, P. Mocarelli, L. Needham, N. Caporaso, and J. Grassman. 2003. TCDD-mediated alterations in the AhR-dependent pathway in Seveso, Italy, 20 years after the accident. *Carcinogenesis* 24:673-80.

91. Institute of Medicine. 1994. Veterans and Agent Orange: Health effects of herbicides used in Vietnam. National Academy Press: Washington, DC.

92. Institute of Medicine. 1997. Veterans and Agent Orange: Update 1996. National Academy Press: Washington, DC.

93. Information Ventures, I. 1992. Review of literature on herbicides, including phenoxy herbicides and associated dioxins. Vol. XX: Analysis of recent literature on health effects, and Vol. XX: Annotated bibliography of recent literature on health effects. U.S. Veterans Administration, Department of Medicine and Surgery: Washington, DC.

94. Information Ventures, I. 1993. Review of literature on herbicides, including phenoxy herbicides and associated dioxins. Vol. XXI: Analysis of recent literature on health effects, and Vol. XXII: Annotated bibliography of recent literature on health effects. U.S. Veterans Administration, Department of Medicine and Surgery: Washington, DC.

95. Information Ventures, I. 1994. Review of literature on herbicides, including phenoxy herbicides and associated dioxins. Vol. XXIII: Analysis of recent literature on health effects, and Vol. XXIV: Annotated bibliography of recent literature on health effects. U.S. Veterans Administration, Department of Medicine and Surgery: Washington, DC.

96. Institute of Medicine. 1999. Veterans and Agent Orange: Update 1998. National Academy Press: Washington, DC.

97. Institute of Medicine. 2001. Veterans and Agent Orange: Update 2000. National Academy Press: Washington, DC.

98. Patterson, D.G., Jr., J.S. Holler, C.R. Lapeza, Jr., L.R. Alexander, D.F. Groce, R.C. O'Conner, S.J. Smith, J.A. Liddle, and L.L. Needham. 1987. High-resolution gas chromatographic/high-resolution mass spectrometric analysis of human serum on a whole-weight and lipid basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Analytical Chemistry* 59(15):2000-5.

99. U.S. Centers for Disease Control. 1988. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in US Army Vietnam-era veterans. The Centers for Disease Control Veterans Health Studies. *The Journal of the American Medical Association* 260(9):1249-54.

100. Kang, H.K., K.K. Watanabe, J. Breen, J. Remmers, M.G. Conomos, J. Stanley, and M. Flicker. 1991. Dioxins and dibenzofurans in adipose tissue of U.S. Vietnam veterans and controls. *American Journal of Public Health* 81(3):344-9.

101. Michalek, J.E., W.H. Wolfe, J.C. Miner, T.M. Papa, and J.L. Pirkle. 1995. Indices of TCDD exposure and TCDD body burden in veterans of Operation Ranch Hand. *Journal of Exposure Analysis and Environmental Epidemiology* 5(2):209-23.

102. Michalek, J.E., J.L. Pirkle, S.P. Caudill, R.C. Tripathi, D.G. Patterson, Jr., and L.L. Needham. 1996. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 10-year followup. *Journal of Toxicology and Environmental Health* 47(3):209-20.

103. Michalek, J.E, A.J. Rahe, P.M. Kulkarni, and R.C. Tripathi. 1998. Levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in 1,302 unexposed Air Force Vietnam-era veterans. *Journal of Exposure Analysis and Environmental Epidemiology* 8(1):59-64.

104. Needham, L.L., P.M. Gerthoux, D.G. Patterson, P. Brambilla, J.L. Pirkle, P.I. Tramaccre, W.E. Turner, C. Beretta, E.J. Sampson, and P. Mocarelli. 1994. Half-life of 2,3,7,8-tetrachlorodibenzo-p-dioxin in serum of Seveso adults: Interim report. *Organohalogen Compounds* 21:81-5.

105. Flesch-Janys, D., P. Gurn, D. Jung, J. Konietzke, and O. Papke. 1994. First results of an investigation of the elimination of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/F) in occupationally exposed persons. *Organohalogen Compounds* 21:93-9.

106. Needham, L.L., P.M. Gerthoux, D.G. Patterson, Jr., P. Brambilla, S.J. Smith, E.J. Sampson, and P. Mocarelli. 1999. Exposure assessment: Serum levels of TCDD in Seveso, Italy. *Environmental Research* 80(2 Pt 2):S200-6.

107. Michalek, J.E, R.C. Tripathi, R.M. Kulkarni, and J.L. Pirkle. 1996. The reliability of the serum dioxin measurement in veterans of Operation Ranch Hand. *Journal of Exposure Analysis and Environmental Epidemiology* 6(3):327-38.

108. Michalek, J.E, R.C. Tripathi, S.P. Caudill, and J.L. Pirkle. 1992. Investigation of TCDD half-life heterogeneity in veterans of Operation Ranch Hand. *Journal of Toxicology and Environmental Health* 35(1):29-38.

109. Fingerhut, M.A., M.H. Sweeney, D.G. Patterson, Jr., L.A. Piacitelli, J.A. Morris, D.A. Marlow, R.W. Hornung, L.W. Cameron, L.B. Connally, L.L. Needham, and W.E. Halperin. 1989. Levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the serum of U.S. chemical workers exposed to dioxin contaminated products: Interim results. *Chemosphere* 19:835-40.

110. Schecter, A., H. McGee, J. Stanley, and K. Boggess. 1992. Dioxin, dibenzofuran, and PCB, including coplanar PCB levels in the blood of Vietnam veterans in the Michigan Agent Orange Study. *Chemosphere* 24:205-8.

111. Piacitelli, L.A., M.H. Sweeney, M.A. Fingerhut, D.G. Patterson, W.E. Turner, L.B. Connally, K.K. Wille, and B. Tompkins. 1992. Serum levels of PCDDs and PCDFs among workers exposed to 2,3,7,8-TCDD contaminated chemicals. *Chemosphere* 25:251-4.

112. Pirkle, J., and V. Houk. 1992. Use of epidemiologic studies to assess human risk from exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Chemosphere* 25:1109-16.

113. Sweeney, M.H., M.A. Fingerhut, D.G. Patterson, Jr., L.B. Connally, L.A. Piacitelli, J.A. Morris, A.L. Greife, R.W. Hornung, D.A. Marlow, J.E. Dugle, W.E. Halperin, and L.L. Needham. 1990. Comparison of serum levels of 2,3,7,8-TCDD in TCP production workers and in an unexposed comparison group. *Chemosphere* 20:993-1000.

114. Schecter, A., H. McGee, J.S. Stanley, and P. Brandt-Rauf. 1996. Dioxins and dioxin-like chemicals in blood and semen of American Vietnam veterans from the state of Michigan. *American Journal of Industrial Medicine* 30(6):647-54.

115. Leem, J.H., Y.C. Hong, K.H. Lee, H.J. Kwon, Y.S. Chang, and J.Y. Jang. 2003. Health survey on workers and residents near the municipal waste and industrial waste incinerators in Korea. *Industrial Health* 41:181-88.

116. Iida, T., and T. Todaka. 2003. Measurement of dioxins in human blood: Improvement of analytical method. *Industrial Health* 41:197-204.

117. Ott, M.G., P. Messerer, and A. Zober. 1993. Assessment of past occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin using blood lipid analyses. *International Archives of Occupational and Environmental Health* 65(1):1-8.

118. Zober, A., and O. Papke. 1993. Concentrations of PCDDs and PCDFs in human tissue 36 years after accidental dioxin exposure. *Chemosphere* 27:413-8.

119. Flesch-Janys, D., J. Berger, J. Konietzko, A. Manz, S. Nagel, and J. Wahrendorf. 1992. Quantification of exposure to dioxins and furans in a cohort of workers of an herbicide producing plant in Hamburg, FRG. *Chemosphere* 25:1021-8.

120. Schecter, A., J. J. Ryan, O. Papke, M. Ball, and A. Lis. 1993. Elevated dioxin levels in the blood of male and female Russian workers with and without chloracne 25 years after phenoxyherbicide exposure: The UFA "Khimprom" incident. *Chemosphere* 27:253-8.

121. Fedorov, L. A. 1993. Dioxin problem in Russian chemical industry. *Chemosphere* 27:477-81.

122. Smith, A.H., D.J. Patterson, M. Warner, R. MacKenzie, and L. Needham. 1992. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels of New Zealand pesticide applicators and their implication for cancer hypotheses. *Journal of the National Cancer Institute* 84(2):104-8.

123. Neuberger, M., W. Landvoigt, and F. Derntl. 1991. Blood levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in chemical workers after chloracne and in comparison groups. *International Archives of Occupational and Environmental Health* 63(5):325-8.

124. Johnson, E.W., W. Parsons, C.R. Weinberg, D.L. Shore, J. Mathews, D.G. Patterson, and L.L. Needham. 1992. Current serum levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in phenoxy acid herbicide applicators and characterization of historical levels. *Journal of the National Cancer Institute* 84(21):1648-53.

125. Mocarelli, P., L.L. Needham, A. Marocchi, D.G. Patterson, Jr., P. Brambilla, P.M. Gerthoux, L. Meazza, and V. Carreri. 1991. Serum concentrations of 2,3,7,8-tetrachlorodibenzo-p-dioxin and test results from selected residents of Seveso, Italy. *Journal of Toxicology and Environmental Health* 32(4):357-66.

126. Ott, M.G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29(9-11):2423-37.

127. Sweeney, M.H., M.A. Fingerhut, J.C. Arezzo, R.W. Hornung, and L.B. Connally. 1993. Peripheral neuropathy after occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *American Journal of Industrial Medicine* 23(6):845-58.

128. Peper, M., M. Klett, R. Frentzel-Beyme, and W.D. Heller. 1993. Neuropsychological effects of chronic exposure to environmental dioxins and furans. *Environmental Research* 60(1):124-35.

129. Patterson, Jr., D.G., M.A. Fingerhut, D.W. Roberts, L.L. Needham, M.H. Sweeney, D.A. Marlow, J.S. Andrews, Jr., and W.E. Halperin. 1989. Levels of polychlorinated dibenzo-p-dioxins and dibenzofurans in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *American Journal of Industrial Medicine* 16(2):135-46.

130. Garrow, J.S., and J. Webster. 1985. Quetelet's index (W/H^2) as a measure of fatness. *International Journal of Obesity* 9:147-53.

131. World Health Organization. 1995. Physical status: The use and interpretation of anthropometry. WHO Technical Report Series. Geneva, Switzerland: World Health Organization.

132. Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L. R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

133. Williamson, D.F. 1993. Descriptive epidemiology of body weight and weight change in U.S. adults. *Annals of Internal Medicine* 119(7 Pt 2):646-9.

134. Pincus, T: 1984. Formal education level—A marker for the importance of behavioral variables in the pathogenesis, morbidity, and mortality of most diseases. *Journal of Chronic Diseases* 311:552.

135. Leistikow, B.N. 2000. The human and financial costs of smoking. *Clinics in Chest Medicine* 21(1):189-97.

136. Appel, D.W., and T.K. Aldrich. 2003. Smoking cessation in the elderly. *Clinics in Geriatric Medicine* 19(1):77-100.

137. Centers for Disease Control and Prevention, National Center for Health Statistics. 2002. Prevalence of overweight and obesity among adults: United States, 1999-2000. U.S. Department of Health and Human Services: Hyattsville, MD.

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10 NEOPLASIA ASSESSMENT

10.1 INTRODUCTION

10.1.1 Background

10.1.1.1 Organs/Diseases

The Air Force Health Study (AFHS) included questionnaire, clinical assessments, and chest x-ray films to ascertain benign and malignant neoplasms. Medical records review was accomplished to confirm reported neoplasms and to identify any unreported neoplasms. In addition, when chest x-ray findings were reported as needing follow-up, the AFHS made every effort to contact and encourage participants to see their physicians and to determine a final diagnosis.

The AFHS evaluation of neoplasms distinguished between skin and systemic neoplasms, and both skin and systemic neoplasms were examined according to the following behavior types: all neoplasms, malignant neoplasms, benign neoplasms, and neoplasms of an unspecified nature. Malignant systemic neoplasms were analyzed according to specific sites. Finally, the prostate-specific antigen (PSA) levels were measured to detect prostate enlargement and prostate cancer.

The neoplasia assessment was based on the occurrence of neoplasms (both benign and malignant) after service in Southeast Asia (SEA). Information on the occurrence of neoplasms at the 1982 baseline examination and at the 1985, 1987, 1992, and 1997 follow-up examinations were coded according to conventions in the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) manual. This information was combined with data collected at the 2002 follow-up examination to form a complete neoplastic history for each participant. The analyses performed in this chapter were based on the 1,951 participants who attended the 2002 follow-up examination.

Cancers are considered to be related to a complex interplay between intrinsic (i.e., inherited genes, hormones, and immunologic mechanisms) and environmental factors. A number of lifestyle factors play a primary role in the etiology of cancers, including dietary constituents, tobacco use, patterns of reproduction, and alcohol consumption. In addition, infectious agents, workplace exposures, natural physical exposures, water and air pollution, medical products and procedures, and consumer products may contribute to an increased risk of developing cancer (1). Tobacco use has long been known to be a major risk factor for lung and laryngeal cancers and is suspected in the etiology of cancers of the bladder, liver, uterine cervix, and perhaps, breast (1). Arsenic, asbestos, benzene, cadmium, and vinyl chloride are among a variety of chemicals known to be human carcinogens (1). Also, a number of viruses, such as the Epstein-Barr herpesvirus, human papillomavirus, hepatitis B and C viruses, and the human immunodeficiency virus (1), are believed to contribute to the development of cancer.

10.1.1.2 Toxicology

Between 1977 and 1988, long-term exposure studies in experimental animals established the multiorgan carcinogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin) (2-9). The carcinogenic response to dioxin occurs in multiple strains and species, in both sexes, and by several routes of administration: dermal (6), feeding (2, 3, 10), gavage (4, 5, 7), and intraperitoneal injection (8). Dioxin has been considered a "complete" carcinogen solely responsible for a variety of malignant tumors at multiple sites (11). The affected sites and exposure needed to induce cancer at these sites varied

substantially from species to species (12, 13), and carcinogenic response varied by exposure rate (14). In rats, dioxin produced tumors of the liver, thyroid, adrenal cortex, lung, nasopharynx, tongue, brain, kidney, and breast (2, 3, 5); in mice, tumors of the liver, thymus, breast, stomach, and skin (4-7, 14); and in the Syrian Hamster, a squamous cell carcinoma of the skin (8). The histopathologic characteristics of the neoplastic response demonstrated greater variety—more than 30 distinct malignancies were characterized microscopically (15).

The biological basis for the assessment of risk related to dioxin exposure has been discussed in several molecular, biological, and pharmacologic studies and reviews (16-30). Experimental studies support an indirect, nongenotoxic mechanism of carcinogenicity of dioxins (26). The biological mechanisms for carcinogenicity, however, have not been firmly established (12, 26). Much of the basic research into the carcinogenicity of dioxin in laboratory animals focused on the properties of the aryl hydrocarbon (Ah) receptor and the induction of the cytochrome P-450 enzyme system (16, 28, 31-36). The Ah receptor was isolated from the tissues of several human organs (37-40) and the comparative properties of animal and human receptors were studied (41, 42). These experiments demonstrated far fewer Ah receptor sites and a significant reduction in dioxin binding affinity in human cells relative to rodent cell lines (23). Experimental animal models showed that health effects mediated by the Ah receptor are similar to those found in exposed human populations, and humans and animals appear to have similar degrees of sensitivity to dioxin-induced effects (25). In a random sample of individuals from Seveso, Italy, 20 years after the Seveso accident in 1976, an analysis of the expression of dioxin-inducible genes involved in carcinogenesis showed that serum dioxin levels are associated with a disrupted regulation of the Ah receptor (43).

10.1.1.3   *Epidemiology*

Many of the longitudinal studies of dioxin toxicity included malignancies as clinical endpoints based on cohorts of civilian populations exposed to dioxin through environmental contamination (43-59), occupation (60-107), and in association with service in SEA during the Vietnam War (108-128). Much debate has taken place over the carcinogenicity of dioxin, and results described in these epidemiologic studies have been the subject of considerable commentary and review (129-177).

One of the most extreme human exposures to dioxin occurred consequent to the industrial explosion in Seveso, Italy, in 1976 (43-53, 59). In the area closest to the explosion, soil concentrations of dioxin ranged from 15.5 to 580.4 $\mu g/m^2$, with a median serum dioxin level of 447 parts per trillion (ppt) measured immediately among residents after the accident (45). Median serum dioxin levels were lower in study areas farther away from the accident site, ranging from 5.5 ppt in unexposed referents to 94 ppt in the second-most contaminated area (45). In a mortality follow-up of this population through 1996, some indication for an increased risk of mortality from respiratory and lymphohematopoietic cancers was found among residents in the most (n=804) and second-most (n=5,941) contaminated areas as compared to the unexposed population, but consistent exposure-response gradients with time since first exposure were not observed. Males were found to have an increased risk of mortality from cancers of the rectum and lung, whereas females showed an increased risk of lymphatic and hematopoietic cancers (45). An earlier cancer incidence study suggested evidence for an elevated risk of hepatobiliary neoplasms and cancers of the hematopoietic system among inhabitants of the second-most contaminated area as compared to the reference population (46).

Other studies of environmental contamination also indicated an elevated risk of some cancers in relation to potential dioxin exposure (54-58). An increased risk of soft tissue sarcoma, which was hypothesized to be at least, in part, related to potential dioxin exposure (54), was found among a population of about 10,000 residents living near a chemical plant in Mantua, Italy. Elevated rates of soft tissue sarcoma and

non-Hodgkin's lymphoma were also found in a population living near a French municipal solid waste incinerator with high emission levels of dioxin (57, 58). Other studies found an increased risk of developing cancer of the lung in populations living near a chemical plant in Russia (56), and of mortality from all cancers combined near a municipal solid waste incinerator in Japan (55).

Carcinogenicity of occupational exposure to dioxins was primarily evaluated in nine worker cohorts in studies conducted by the International Agency for Research on Cancer (IARC) (80-82, 90) and the National Institute for Occupational Safety and Health (NIOSH) (74, 91, 92, 107), as well as in studies of production workers at Dow Chemical Company (63-65, 70-72, 86, 87, 89, 106), Monsanto (69, 95, 104), BASF (85, 88, 93, 96-98), and in the Netherlands (66, 79), Germany (60-62, 76-78), Britain (68, 103), and Denmark (101, 102). The IARC study included the Dutch, German, British, and Danish workers, whereas the NIOSH cohort included workers studied separately in the Dow Chemical Company and Monsanto studies.

The most recent update of the IARC follow-up study, published in 1997, evaluated the mortality of 21,863 male and female workers exposed to dioxins in 12 countries from 1939 to 1992 (80). Elevated risks of cancer mortality from the kidney, bladder, female breast, respiratory organs, and connective tissue and other soft tissues were observed among workers exposed to dioxins. The risk of mortality from all malignant neoplasms, lung cancer, and non-Hodgkin's lymphoma was slightly increased, but no relation with duration of exposure was found (80). A case-control study of 11 cases and 55 controls nested within this cohort found an excess risk of soft tissue sarcoma in relation to dioxin exposure (81).

Two cohorts included in the IARC study evaluated cancer risk in relation to serum dioxin levels. In the German study of 1,189 male workers involved in the production of herbicides and insecticides, cancer mortality was evaluated from 1952 through 1992 (62, 77, 78). An average serum dioxin level of 108.6 ppt was observed. Total cancer mortality was elevated in a dose-response fashion, whereas risks were elevated for neoplasms of the lung and lymphohematopoietic system, but inconsistently related to serum dioxin levels (62, 78). In a 1998 update of the Dutch cohort of 1,167 workers from 1955 through 1991, reported average serum dioxin levels were 7.6 ppt in unexposed workers and ranged from 16.6 to 96.3 ppt in those exposed. Some indication of an exposure-related cancer risk was found (79).

As part of the NIOSH Dioxin Registry, cause-specific mortality was initially determined in 5,172 workers exposed to dioxin at 12 U.S. chemical production plants (74). Serum dioxin levels were measured among 253 members of the exposed cohort and in 79 unexposed persons; average serum dioxin levels were 233 ppt and 7 ppt, respectively (74). Updates of this cohort extended the period of follow-up by 6 years through 1993. Analyses in these studies were restricted to 3,538 workers in eight plants for whom estimated (92) or blood-measured (91) levels of dioxin exposure could be determined and co-exposure to pentachlorophenol could be ruled out. The estimated dioxin exposure that was used estimated air exposure levels and known serum dioxin levels from 170 workers based on the employment history of each worker, the estimated half-life for dioxin, and a pharmacokinetic model for the storage and excretion of dioxin (91, 107). The initial evaluation found an excess mortality from all cancers, lung cancer, and soft tissue sarcoma (74). Mortality was elevated for cancers of the larynx, lung, bladder, and connective tissue and soft tissue among workers with chloracne (92). The risk of mortality from all cancers combined and lung cancer was highest among those with the highest cumulative exposure estimates (91, 92, 107). Individual studies of workers at Dow Chemical Company and Monsanto were smaller and did not assess mortality in relation to estimated serum dioxin levels (63-65, 69-72, 86, 87, 89, 95, 104, 106).

A follow-up study (1953-1992) of 243 German factory workers exposed to dioxin during a chemical explosion in 1953 reported that median serum dioxin levels ranged from 148 ppt among workers without chloracne to 1,118 ppt among those with severe chloracne (88, 98). An exposure-related increase in

mortality from all cancers combined was observed based on a total of 31 cases. Furthermore, an increased risk of lung cancer was found among those with the highest exposure to dioxins. Little evidence was seen for an increased risk of mortality or morbidity from any other cancer site (88).

The AFHS is unique among studies that have examined the incidence of malignancy in Vietnam veterans because serial serum dioxin data have been incorporated into longitudinal analyses (115, 117, 118, 122, 125, 128, 178). During the 1987 and 1992 examinations, the median serum dioxin level in the Ranch Hand cohort was nearly three times that of the Comparison group (12.5 ppt versus 4.1 ppt) (125). Stratification of the Ranch Hand cohort by occupation revealed significantly higher median levels of serum dioxin in the enlisted groundcrew (24.1 ppt) and enlisted flyers (17.8 ppt) than in the officers (7.7 ppt) (125). Each veteran was assigned to a background, low, or high dioxin exposure category based on serum dioxin levels.

The risk of developing skin and systemic cancers was evaluated in an AFHS article based on data collected through the 1992 examination (115). No increased skin cancer risk was found in Ranch Hands with the highest levels of serum dioxin, nor was there any consistent evidence of a dose-response effect (115). Elevated but not statistically significant risks were observed for oropharyngeal neoplasms and cancers of kidney or bladder among Ranch Hands with elevated exposure. Analyses assessing cancer risk by time since end of service did not reveal any consistent patterns (115). Similar results were reported in the 1997 follow-up examination (128). Another analysis conducted in 1998 evaluating post-service mortality among Ranch Hands found little evidence for an elevated risk of mortality from any cancer (118).

An article published in 2004 that describes cancer in AFHS participants explored the effects of time spent in SEA, the calendar period of service, and the percentage of SEA service spent in Vietnam (179). The analysis included external contrasts against U.S. national cancer rates and internal analyses by dioxin exposure category (similar to the Model 3 analyses in this report). Cancer incidence and mortality were separately considered. Cancer morbidity was classified by anatomical site using definitions provided by the Surveillance, Epidemiology, and End Results (SEER) section of the National Cancer Institute. The SEER categories included all anatomical sites except basal cell and squamous cell carcinoma. External contrasts found that the incidence of melanoma and prostate cancer was significantly increased among white Ranch Hand veterans; relative risks were increased and remained significant after restriction to participants whose tour of duty occurred between 1966 and 1970, the period of heaviest Agent Orange spraying. No significant increases in cancer mortality were found relative to national rates. Two internal analyses were conducted: the first was restricted to participants who spent at most 2 years in SEA and the second to Ranch Hands who spent 100 percent of their SEA tour in Vietnam and to Comparisons who spent 0 percent of their SEA tour in Vietnam. Among Ranch Hands who spent at most 2 years in SEA, the risk of cancer at any SEER site was significantly increased in the low and high dioxin categories relative to Comparisons who spent at most 2 years in SEA. Among Ranch Hands who spent 100 percent of their SEA tour in Vietnam, the risk of cancer at any SEER site was significantly increased in the low and high dioxin categories relative to Comparisons who spent 0 percent of their SEA tour in Vietnam. Consideration of these and other factors came too late for inclusion in this report.

Studies of cancer risk among Vietnam veterans have yielded inconsistent findings. Some studies reported increased cancer risks among Vietnam veterans (109, 119-121), while others found no evidence suggesting elevated risks (108, 111-114, 116, 123).

The Institute of Medicine (IOM), as reported first in their 1994 book on the health effects of herbicides used in Vietnam (180), concluded that there is "sufficient" evidence to establish an association, although not a causal relation, between dioxin exposure and the occurrence of soft tissue sarcoma, non-Hodgkin's

lymphoma, and Hodgkin's disease (12, 180-183). In the 2002 IOM report, the epidemiologic evidence was considered to be sufficient concerning chronic lymphocytic leukemia based primarily on studies of agricultural workers (12). The evidence for an association with respiratory cancers, prostate cancer, and multiple myeloma was considered "limited/suggestive" (12, 180-183).

10.1.2   Summary of Previous Analyses of the Air Force Health Study

10.1.2.1   *1982 Baseline Examination Summary Results*

Cancer received major emphasis during the AFHS baseline examination in 1982. The neoplasia assessment used data from both the in-home questionnaire and the review-of-systems questionnaire obtained during the physical examination, as well as data from the examination itself. In addition, tabulation of mortality count data from the baseline mortality report was used in conjunction with cancer morbidity information. The overall results did not show a significant difference in systemic cancer between the two groups, but did show significantly more skin cancer in the Ranch Hand group.

Of 50 reported systemic cancers from the Ranch Hand and Comparison groups, 28 (14 in each group) were verified by medical records and pathology reports. Although the number of occurrences was too small to support meaningful statistical analysis, a slight excess of genitourinary cancer and oropharyngeal cancer, but a decrease of digestive system neoplasms, were observed for Ranch Hands. A combined morbidity-mortality assessment derived from the initial 1:1 match (Ranch Hand to the Original Comparison member) disclosed similar distributions. One case of soft tissue sarcoma and one case of Hodgkin's disease were confirmed, both in the Comparison group.

Questionnaire data verified by a medical records review revealed significantly more skin cancer in Ranch Hands. Basal cell carcinoma accounted for 83.9 percent of the reported skin cancers in both groups and was concentrated anatomically on the face, head, and neck. The few melanoma and squamous cell cancers were distributed evenly between the Ranch Hand and Comparison groups. Adjustments for occupational exposures (e.g., asbestos, degreasing chemicals) did not alter the increased rate of skin cancer in the Ranch Hand group. Outdoor occupations subsequent to military service as a covariate did not account for the significant skin cancer association.

10.1.2.2   *1985 Follow-up Examination Summary Results*

The baseline and 1985 follow-up data were combined for the assessment of lifetime history of cancer. The adjusted group contrast between Ranch Hands and Comparisons for the sun exposure-related skin cancers, the majority of which were basal cell carcinomas, was significant. The group contrasts for all systemic cancers combined were not significant. There was one new occurrence of a soft tissue sarcoma (Ranch Hand) and one suspected cancer of the lymphatic system (Ranch Hand), in addition to the one previously reported soft tissue sarcoma and one Hodgkin's disease in the Comparison group. There were no cases of non-Hodgkin's lymphoma in either group at the time of the 1985 report.

10.1.2.3   *1987 Follow-up Examination Summary Results*

For non-Black participants, significantly more Ranch Hands had a skin neoplasm than did Comparisons. The majority of malignant neoplasms observed in Ranch Hands were basal cell carcinomas, a nonlife-threatening form of skin cancer. Ranch Hands exhibited a significantly increased risk for sun exposure-related malignant skin neoplasms. Approximately 90 percent of the participants with a sun exposure-related malignant skin neoplasm had a basal cell carcinoma.

After adjusting for age, residential history, sun exposure, ethnic background, and ionizing radiation exposure, the Ranch Hand risk was statistically significantly increased for verified basal cell carcinoma. Also, a significantly higher percentage of Ranch Hands had multiple verified basal cell carcinomas than did Comparisons.

No significant group differences were found in the analyses of systemic neoplasms by number, behavior (malignant, benign, or uncertain behavior or unspecified nature), or site. Thus, the increase in overall malignancy was because of elevated relative risks for skin cancer (basal cell carcinoma). The number of participants with soft tissue sarcoma and non-Hodgkin's lymphoma was comparable in the two groups.

10.1.2.4   *Serum Dioxin Analysis of 1987 Follow-up Examination Summary Results*

The analyses did not establish a positive association between dioxin and the presence of a skin neoplasm. Significant relative risks were found for the skin neoplasm analyses, although the relative risks were almost always inversely related to dioxin levels. For the analyses focusing on enlisted flyers with a basal cell carcinoma on sites other than the ear, face, head, or neck (and a sun exposure-related malignant skin neoplasm on sites other than the ear, face, head, or neck), relative risks were found to be significantly greater than 1.0. These differences were not noted in the enlisted groundcrew who, as a group, had higher levels of serum dioxin than enlisted flyers.

The relative risk for participants with a benign systemic neoplasm (such as lipomas) increased as the different measures of dioxin (initial, categorized, and 1987) increased. The relative risk of malignant systemic neoplasms was not significantly increased as dioxin levels increased.

The study provided no evidence of increased history of malignant neoplasms most commonly suspected as being associated with exposure to chlorophenols (Hodgkin's disease, non-Hodgkin's lymphoma, and soft tissue sarcoma). The number of participants with these specific malignancies was small; therefore, the statistical power to detect small or moderately elevated relative risks was low. The data do not support evidence of a relation between dioxin and either skin or systemic malignancies.

10.1.2.5   *1992 Follow-up Examination Summary Results*

Analyses of all Ranch Hands and Comparisons indicated no significant difference between the two groups with regard to benign or malignant neoplasms. All statistically significant associations between initial dioxin and benign or malignant neoplasm endpoints for Ranch Hands showed an inverse dose-response relation. After adjusting for covariates, the only significantly increased risks were for Ranch Hands in the low category for all skin neoplasms and malignancies of the colon and rectum. In contrast, the occurrence of neoplasms of any type for Ranch Hands in the high dioxin category was never significantly elevated and was often less than the occurrence for Comparisons. Parallel to analyses using initial dioxin, results observed when 1987 dioxin was used as the measure of exposure often indicated an inverse dose-response relation, although this was statistically significant in the adjusted analyses only for benign skin neoplasms. In summary, there appeared to be no overall difference between Ranch Hands and Comparisons, and there was no evidence to suggest a positive dose-response relation between dioxin and neoplastic disease.

10.1.2.6   *1997 Follow-up Examination Summary Results*

Several analyses showed significantly more Ranch Hands than Comparisons with a history of malignant skin or systemic neoplasms; however, no significant results were found within the enlisted groundcrew stratum, the military occupational category believed to have been, on average, the most heavily exposed.

When the association between initial dioxin and malignant neoplasms was examined within Ranch Hands, the neoplasm occurrence decreased as initial dioxin increased. A significant increase of malignant neoplasms for Ranch Hands in the low dioxin category relative to Comparisons was observed, but there was no such increase in Ranch Hands in the high dioxin category. In summary, Ranch Hands did not exhibit a significantly increased risk for neoplastic disease, nor did they show a positive dose-response relation between dioxin and malignant neoplastic conditions.

10.1.3 Parameters for the 2002 Neoplasia Assessment

10.1.3.1 Dependent Variables

The neoplasia assessment was based on the occurrence of neoplasms (both benign and malignant) after service in SEA. Information on the occurrence of neoplasms at the 1982 baseline examination and at the 1985, 1987, 1992, and 1997 follow-up examinations were coded according to conventions in the ICD-9-CM manual. This information was combined with data collected at the 2002 follow-up examination to form a complete neoplastic history for each participant. The analyses performed in this chapter were based on the 1,951 participants who attended the 2002 follow-up examination.

The neoplasia assessment was based on the number of participants with a neoplasm and not on the number of neoplasms. A participant was considered to have an adverse health condition for the neoplasia assessment if he had one or more neoplasms.

10.1.3.1.1 Medical Records Variables

During the 2002 health interview, each study participant was asked a series of questions on the occurrence of cancer since the date of his last health interview. Medical records review was accomplished to confirm reported neoplasms and to identify any unreported neoplasms. These data from the 2002 physical examination were combined with data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations to form a complete neoplasia history for each participant. Only verified neoplasms were used in the neoplasia assessment.

Some possible neoplastic conditions were discovered by the physicians at the physical examination. Contingent upon participant authorization, suspicious skin lesions were biopsied and the pathology determined; no other invasive procedures were used to detect systemic neoplasms. A skin biopsy was indicated for 307 of the 1,951 (15.7%) participants at the 2002 follow-up examination; 289 of these 307 participants (94.1%) consented to the biopsy.

For chest x-ray findings that were reported as needing follow-up at the 2002 physical examination, the AFHS made every effort to contact and encourage participants to see their physicians. The participants were recontacted to determine a final diagnosis. Results that were available upon follow-up were included in the analysis of neoplasms in this chapter.

10.1.3.1.1.1 Skin Neoplasms

The analysis of skin neoplasms was divided into two sets. The first set comprised analyses of skin neoplasms by behavior. Four behavior types were examined: (1) all skin neoplasms, (2) malignant skin neoplasms only, (3) benign skin neoplasms only, and (4) skin neoplasms of uncertain behavior or unspecified nature.

The second set comprised analyses of malignant skin neoplasms by cell type and was conducted for all sites combined. The following four cell types were analyzed: (1) basal cell carcinomas, (2) squamous cell carcinomas, (3) nonmelanoma (basal cell carcinomas, squamous cell carcinomas, and malignant epithelial neoplasms not otherwise specified), and (4) melanoma.

There were relatively few Black participants in this study (6.4%). With the exception of one Black participant with a pre-SEA melanoma in a previous follow-up examination, Blacks have been observed to exhibit only benign skin neoplasms in all phases of the study to date. Consequently, skin neoplasm analyses, except for the analyses of benign skin neoplasms, were limited to non-Black participants. Both Black and non-Black participants were included in the analysis of benign skin neoplasms. Participants with a pre-SEA skin neoplasm were excluded from the analysis of the skin neoplasm variables.

10.1.3.1.1.2   Systemic Neoplasms

The systemic neoplasms were analyzed by behavior and anatomical site. As with skin neoplasms, each analysis was conducted using verified data. The analysis of the systemic neoplasms was divided into two sets, as described below.

The first set comprised analyses of systemic neoplasms by behavior type. The following four behavior types were examined: (1) all systemic neoplasms, (2) malignant systemic neoplasms, (3) benign systemic neoplasms, and (4) systemic neoplasms of uncertain behavior or unspecified nature.

The second set comprised analyses of malignant systemic neoplasms by the following sites: (1) ear, eye, head, face, and neck; (2) oral cavity, pharynx, and larynx; (3) thymus, heart, and mediastinum; (4) thyroid gland; (5) bronchus and lung; (6) colon and rectum; (7) urinary system; (8) kidney and ureter; (9) prostate; (10) penis and other male genital organs; (11) testicles; (12) bone and articular cartilage; (13) connective and other soft tissues, (14) carcinoma in situ, (15) all stomach neoplasms (malignant and benign), (16) Hodgkin's disease, (17) leukemia, (18) malignant systemic neoplasm of lymphoid and histiocytic tissue, and (19) lymphoreticular sarcoma.

Participants with a pre-SEA malignant systemic neoplasm or a pre-SEA systemic neoplasm of uncertain behavior or an unspecified nature were excluded from the analysis of the systemic neoplasm variables.

10.1.3.1.1.3   Skin and Systemic Neoplasms

Statistical analysis was performed on malignant neoplasms, which was a combination of malignant skin and malignant systemic neoplasms. In addition, statistical analysis was performed on all neoplasms, which was a combination of skin and systemic neoplasms (benign, malignant, and uncertain behavior). Participants with a pre-SEA skin neoplasm, a pre-SEA malignant systemic neoplasm, or a pre-SEA systemic neoplasm of uncertain behavior or an unspecified nature were excluded from the analysis of this variable.

10.1.3.1.2 Laboratory Variable

The PSA test was developed to detect prostate enlargement and prostate cancer. Each participant had a PSA test as a standard part of the laboratory assay. An analysis was performed on the continuous measurement, as measured in ng/mL, as well as on a discrete form of PSA. The discrete form of PSA was categorized as high or normal based on a cutpoint of 4 ng/mL. Participants with prostatectomies or radiation treatment on the prostate were excluded from the analysis of PSA.

10.1.3.2   Covariates

In the analysis of the 2002 examination results, covariates in adjusted statistical analyses assessing skin neoplasms included age, military occupation, body mass index (kg/m^2), skin color, hair color, eye color, skin reaction to sun after the first exposure, skin reaction to sun after repeated exposure, cumulative exposure to ionizing radiation (yes or no), cumulative exposure to industrial chemicals (yes or no), and average lifetime residential history. A composite skin-reaction index, which combined two individual reactions of skin to sun covariates, also was investigated.

Age, race, and military occupation were determined from military records. Body mass index was calculated as weight/(height)^2, where the weight was measured in kilograms and the height was measured in meters at the physical examination (184). For purposes of covariate associations for discrete dependent variables, body fat was dichotomized as "not obese" (≤ 30 kg/m^2) and "obese" (>30 kg/m^2).

Information on skin, hair, and eye color was obtained at the 2002 physical examination for participants who did not attend the 1985, 1987, 1992, and 1997 examinations. This information was combined with data from participants who previously provided this information. Information on the skin reaction to sun after the first exposure and after repeated exposure was reported by the participant during the questionnaire phase at the 2002 examination. Also, the participants' cumulative exposures through 1997 to ionizing radiation, industrial chemicals, and herbicides (used in the analysis of systemic neoplasms, discussed below) were updated with information reported in the 2002 questionnaire.

The emphasis on choosing risk factors related to cancer increased during the 1985 follow-up examination and has been emphasized since that time. In particular, the interval health questionnaire was modified to collect information on each geographic location in which a participant lived for more than 12 months. Because ultraviolet light exposure has been acknowledged as the primary cause of basal cell carcinomas, this information was used to compute a cumulative sun-exposure index based on residential history. An average lifetime residential history was estimated by dividing the total degree-years (i.e., the sum of the product of latitude [degrees] and the number of years lived at each residence) from all residences by the total number of residential years reported on questionnaires since 1985. Average lifetime residential history was dichotomized as less than 37 degrees latitude (southerly) or greater than or equal to 37 degrees latitude (northerly), which was the approximate median in previous AFHS examinations.

Covariates in adjusted statistical analyses assessing systemic neoplasms and PSA included age, race, military occupation, body mass index (kg/m^2), cumulative exposure to ionizing radiation and herbicides, lifetime cigarette smoking history (in pack-years), and lifetime alcohol history (in drink-years).

Lifetime cigarette smoking history was based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 2002 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

Lifetime alcohol history was based on information from the 2002 questionnaire and combined with similar information gathered at the 1987, 1992, and 1997 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking pattern changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year.

Almost all Ranch Hands reported herbicide exposure at some point in their lifetime. Although the questionnaire had been structured to indicate post-SEA exposure only, a possible explanation for this reported herbicide exposure may have been the tendency of Ranch Hands to report their exposure to dioxin during their time of duty in SEA. Consequently, herbicide exposure in Ranch Hands was of limited use as a risk factor for explaining the presence of a systemic neoplasm. Therefore, many of the Model 2 and Model 4 analyses of systemic neoplasms and PSA, which were based on Ranch Hands only, did not use herbicide exposure as a covariate.

Categories of covariates and definitions are summarized below:

- Skin Color: dark, medium, pale, dark peach, and pale peach (classified for analysis purposes as (1) dark, medium, pale, or (2) dark peach, pale peach)

- Hair Color: black, dark brown, light brown, blond, red, and bald (classified for analysis purposes as (1) black, dark brown, or (2) light brown, blond, red, bald)

- Eye Color: brown, hazel, green, gray, and blue (classified for analysis purposes as (1) brown, (2) hazel, green, or (3) gray, blue)

- Skin Reaction to Sun After First Exposure: burns painfully, burns, becomes red, and no reaction

- Skin Reaction to Sun After Repeated Exposure: freckles with no tan, tans mildly, tans moderately, and tans deep brown

- Composite Skin-Reaction Index: a composite variable based on two reactions of skin to sun exposure variables was defined as follows: (1) burns painfully or freckles with no tan, (2) burns or tans mildly, and (3) all other reactions

- Average Lifetime Residential History: average latitude less than 37 degrees and average greater than or equal to 37 degrees

- Exposure to Carcinogens: ionizing radiation, industrial chemicals, and herbicides (yes or no for each); these exposures represent cumulative exposure based on self-reported questionnaire data from the 2002 examination combined with previous examinations.

10.1.4 Statistical Methods

Table 10-1 summarizes the statistical analysis performed for the 2002 neoplasia assessment. The first part of this table identifies the dependent variables, covariates, exclusions, and the statistical methods. This information is presented in the following four sections: skin neoplasms, systemic neoplasms, skin and systemic neoplasms combined, and PSA. Data source, data form, and cutpoints are summarized at the end of the table. The second part of the table describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 10-1.

The neoplasm assessment contains many covariates for use in the adjusted analyses of skin and systemic neoplasms. In addition, the history of a neoplasm was small for many of the dependent variables. The modeling strategy for this clinical area was to include as many covariates as feasible; however, when the number of participants with a history of a particular neoplasm was too small to support analysis including all covariates, elimination of covariates was necessary to develop and support meaningful analyses.

Table 10-1. Statistical Analysis for the Neoplasia Assessment

Dependent Variables

Category	Site (ICD-9-CM Codes [with T codes and M codes])	Covariates[a]	Exclusions[b]
<u>Skin Neoplasms</u>			
Behavior			
All	All Sites Combined (172.0 – 173.9, 176.0, 198.2, 214.0 and 214.1 [only with T codes T01000 - T02990], 216.0 – 216.9, 222.1 [only with T codes T02530 - T02544], 222.4 [only with T code T02545], 228.01 and 228.1 [only with T code T01000 through T02990], 232.0 – 232.9, 238.2, 239.2 [only with T code T01000 through T02990])	(1)	(a)
Malignant	All Sites Combined (172.0 – 173.9, 198.2, 232.0 – 232.9)	(1)	(a)
Benign	All Sites Combined (214.0 and 214.1 [only with T code T01000 through T02990], 216.0 – 216.9, 222.1 [only with T code T02530 through T02544], 222.4 [only with T code T02545], 228.01 and 228.1 [only with T code T01000 through T02990])	(1)	(b)
Uncertain Behavior or Unspecified Nature	All Sites Combined (238.2, 239.2 [only with T code T01000 through T02990])	(1)	(a)
Cell Type-specific Analyses			
Basal Cell Carcinoma	All Sites Combined (173.0 – 173.9, 198.2, 232.0 – 232.9 [with M codes M80903 - M80943])	(1)	(a)
Squamous Cell Carcinoma	All Sites Combined (173.0 – 173.9, 198.2, 232.0 – 232.9 [with M codes M80520 - M80763])	(1)	(a)
Nonmelanoma	All Sites Combined (173.0 – 173.9, 176.0, 198.2, 232.0 – 232.9)	(1)	(a)
Melanoma	All Sites Combined (172.0 – 172.9 [with M codes M87200 – 87903], 232.0 - 232.9 [only with M codes M87202, M87402, M87412, and M87422])	(1)	(a)

Category	Site (ICD-9-CM Codes [with T codes and M codes])	Covariates[a]	Exclusions[b]

Systemic Neoplasms

Behavior

Category	Site (ICD-9-CM Codes [with T codes and M codes])	Covariates[a]	Exclusions[b]
All	All Sites Combined (140.0 – 171.9, 175.0, 175.9, 176.1 – 176.9, 185 – 198.1, 198.3 – 198.5, 198.7 – 208.9, 210.0 – 213.9, 214.0 and 214.1 [with any T code except T01000 through T02990], 214.2 - 215.9, 217, 222.0, 222.1 [with any T code except T02530 through T02544], 222.2 – 222.3, 222.4 [with any T code except T02545], 222.8 – 227.9, 228.00, 228.01 [with any T code except T01000 through T02990], 228.02 - 228.09, 228.1 [with any T code except T01000 through T02990], 229.0 - 231.9, 233.4 – 235.9, 236.4 - 238.1, 238.3 – 239.1, 239.2 [with any T code except T01000 through T02990], 239.3 - 239.9)	(2)	(c)
Malignant	All Sites Combined (140.0 – 171.9, 176.1 – 176.9, 185 – 208.91, 230.0 – 231.9, 233.0, 233.4 –234.9)	(2)	(c)
Benign	All Sites Combined (210.0 – 213.9, 214.0 – 214.1 [with any T code except T01000 - T02990], 214.2 – 215.9, 217, 222.0, 222.1 [with any T code except T02530 through T02544], 222.2 – 222.3, 222.4 [with any T code except T02545], 222.8 – 228.00, 228.01 [with any T code except T01000 through T02990], 228.02 - 229.9)	(2)	(c)
Uncertain Behavior or Unspecified Nature	All Sites Combined (235.0 – 238.1, 238.3 – 239.1, 239.2 [with any T code except T01000 through T02990], 239.3 – 239.9)	(2)	(c)

Site-specific Analyses

Category	Site (ICD-9-CM Codes [with T codes and M codes])	Covariates[a]	Exclusions[b]
Malignant	Eye, Ear, Face, Head, and Neck (160.0 – 160.9, 170.0, 170.1, 171.0, 190.0 – 190.9, 195.0, 234.0, 234.8)	(2)	(c)
Malignant	Oral Cavity, Pharynx, and Larynx (140.0 – 149.9, 161.0 – 161.9, 230.0, 231.0)	(2)	(c)
Malignant	Thymus, Heart, and Mediastinum (164.0, 164.2 – 164.9, 197.1)	(2)	(c)
Malignant	Thyroid Gland (193, 194.1)	(2)	(c)
Malignant	Bronchus and Lung (162.0 – 163.9, 197.0, 197.2, 197.3, 231.1 – 231.9 [includes trachea and pleura])	(2)	(c)
All	Stomach (151.0 – 151.9, 211.1, 230.2, 235.2, 239.0)	(2)	(c)
Malignant	Colon and Rectum (includes anus) (153.0 – 154.8, 197.5, 230.3 – 230.6)	(2)	(c)

Category	Site (ICD-9-CM Codes [with T codes and M codes])	Covariates[a]	Exclusions[b]
Malignant	Urinary System (188.0 – 189.9, 198.0, 198.1, 233.7, 233.9)	(2)	(c)
Malignant	Kidney and Ureter (189.0 – 189.2, 198.0, 233.9)	(2)	(c)
Malignant	Prostate (185, 233.4)	(2)	(c)
Malignant	Penis and Other Male Genital Organs (187.2 – 187.6, 187.8, 187.9, 198.82)	(2)	(c)
Malignant	Testicles (186.0, 186.9, 233.6)	(2)	(c)
Malignant	Bone and Articular Cartilage (170.0 – 170.9, 198.5)	(2)	(c)
Malignant	Connective and Other Soft Tissues (171.0 – 171.9)	(2)	(c)
Pre-malignant	Carcinoma In Situ (Breast, Digestive Organs, Respiratory, Prostate, Penis and Other Male Genitals, and Bladder and Other and Nonspecified Urinary) (230.0 – 231.9, 233.0, 233.4 – 234.9)	(2)	(c)
Malignant	Hodgkin's Disease (201.00 – 201.98)	(2)	(c)
Malignant	Leukemia (204.00 – 208.91)	(2)	(c)
Malignant	Other Malignant Systemic Neoplasms of Lymphoid and Histiocytic Tissue (196.0 – 196.9, 202.10 – 202.68, 203.10 – 203.81)	(2)	(c)
Malignant	Lymphoreticular Sarcoma (200.00 – 200.88)	(2)	(c)

Skin and Systemic Neoplasms

Category	Site (ICD-9-CM Codes [with T codes and M codes])	Covariates[a]	Exclusions[b]
All	All Sites Combined [140.0 – 239.9]	(3)	(d)
Malignant	All Sites Combined [140.0 – 173.9, 175.0 – 176.9, 185.0 – 208.9, 230.0 – 234.9]	(3)	(d)

Variable (Units)	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
PSA					
PSA (ng/mL)	C/D	High: >4 Normal: ≤4	(2)	(e)	U:LR,CS,GLM,TT A:LR,GLM

Dependent Variables (Except for PSA)

Data Source: Review of medical records and verification based on AFHS questionnaires and physical
            examinations, except for PSA, which was measured by Scripps Clinic in 2002.
Data Form: Discrete.
Cutpoints: Yes or No.

Statistical Analysis and Methods:
      Unadjusted: LR: Logistic regression analysis
                  CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
        Adjusted: LR: Logistic regression analysis

[a]Covariates:
(1) age, military occupation, body mass index, skin color, hair color, eye color, skin reaction to sun after first
    exposure, skin reaction to sun after repeated exposure, composite skin-reaction index, residential history,
    cumulative ionizing radiation exposure, and cumulative industrial chemicals exposure.
(2) age, race, military occupation, body mass index, cumulative ionizing radiation exposure, cumulative herbicide
    exposure, lifetime cigarette smoking history, lifetime alcohol history.
(3) age, race, military occupation, body mass index, skin color, hair color, eye color, skin reaction to sun after first
    exposure, skin reaction to sun after repeated exposure, composite skin-reaction index, residential history,
    cumulative ionizing radiation exposure, cumulative industrial chemicals exposure, cumulative herbicide
    exposure, lifetime cigarette smoking history, lifetime alcohol history.

[b]Exclusions:
(a) participants with a pre-SEA skin neoplasm, Blacks.
(b) participants with a pre-SEA skin neoplasm.
(c) participants with a pre-SEA systemic neoplasm of uncertain behavior, participants with a pre-SEA malignant
    systemic neoplasm.
(d) participants with a pre-SEA skin neoplasm, participants with a pre-SEA systemic neoplasm of uncertain
    behavior, participants with a pre-SEA malignant systemic neoplasm.
(e) participants with a prostatectomy or radiation treatment on the prostate gland.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	C/D	Born $\geq$ 1942 Born < 1942
Race	MIL	D	Black Non-Black
Military Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Body Mass Index (kg/m^2)	PE	C/D	Not Obese: ≤ 30 Obese: >30
Cumulative Ionizing Radiation Exposure	Q-SR	D	Yes No
Skin Color	PE	D	Non-Peach: Dark, Medium, Pale Peach: Dark Peach, Pale Peach
Hair Color	PE	D	Black, Dark Brown Light Brown, Blond, Red, Bald

Table 10-1. Statistical Analysis for the Neoplasia Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints
Eye Color	PE	D	Brown Hazel, Green Gray, Blue
Skin Reaction to Sun After First Exposure	Q-SR	D	Burns Painfully Burns Becomes Red No Reaction
Skin Reaction to Sun After Repeated Exposure	Q-SR	D	Freckles with No Tan Tans Mildly Tans Moderately Tans Deep Brown
Composite Skin-reaction Index	Q-SR	D	• Burns Painfully After 2 Hours or Freckles with No Tan After Repeated Exposure • Burns After 2 Hours or Tans Mildly After Repeated Exposure • All Other Reactions
Average Lifetime Residential History	Q-SR	D	Latitude < 37º Latitude ≥ 37º
Cumulative Industrial Chemicals Exposure	Q-SR	D	Yes No
Cumulative Herbicide Exposure	Q-SR	D	Yes No
Lifetime Cigarette Smoking History (pack-years)	Q-SR	C/D	0 >0–10 >10
Lifetime Alcohol History (drink-years)	Q-SR	C/D	0 >0–40 >40

Abbreviations

Data Source:	MIL: Air Force military records PE: 2002 physical examination Q-SR: Health questionnaires (self-reported)
Data Form:	D: Discrete form of dependent variable or covariate C/D: Continuous and discrete forms of dependent variable; appropriate form for analysis (either continuous or discrete) of covariate
Statistical Analysis:	U: Unadjusted analysis A: Adjusted analysis
Statistical Methods:	CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables) GLM: General linear models analysis LR: Logistic regression analysis TT: Two-sample t-test

Four models were examined for each dependent variable given in Table 10-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for covariates. These covariates are given in Table 10-1. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. In an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-4, the median level of exposure to dioxin was highest for enlisted groundcrew, followed by enlisted flyers, then officers.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the Centers for Disease Control and Prevention (CDC) using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in ppt on a lipid weight basis (185). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2. A statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model to account for body mass index-related differences in elimination rate (186).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. Another category was examined by combining the low and high Ranch Hand categories. This combination is referred to in the tables as the "low plus high Ranch Hand" category. These five categories—Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the four Ranch Hand categories and the dependent variable in the Comparison category was examined. As in Model 2, a statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables. One Ranch Hand without a dioxin measure was excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The term "unadjusted" was used in the text and tables as follows: Models 1 and 4 did not adjust for any covariates. Models 2 and 3 adjusted only for body mass index at the time of the blood measurement for dioxin. The term "adjusted" was used in the text and tables as follows: Models 1 and 4 adjusted for the covariates shown in Table 10-1 unless otherwise specified by a footnote to the table. Models 2 and 3 additionally adjusted only for body mass index at the time of the blood measurement for dioxin.

Table 10-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants that were excluded from analyses is given.

Table 10-2. Number of Participants Excluded or with Missing Data for the Neoplasia Assessment

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Body Mass Index	COV	1	0	0	1	1	0
Lifetime Alcohol History	COV	4	5	3	4	4	5
Average Lifetime Residential Latitude	COV	1	3	0	1	1	3
Lifetime Cigarette Smoking History	COV	0	3	0	0	0	3
Skin Reaction to Sun After First Exposure	COV	0	2	0	0	0	2
Skin Reaction to Sun After Repeated Exposure	COV	0	2	0	0	0	2
Composite Skin-Reaction Index	COV	0	2	0	0	0	2
Pre-SEA Skin Neoplasm (malignant, uncertain behavior, benign)	EXC	7	13	4	7	7	13
Pre-SEA Malignant Systemic Neoplasm	EXC	4	0	4	4	4	0
Pre-SEA Uncertain Behavior Systemic Neoplasm	EXC	5	2	3	5	5	2
Pre-SEA Neoplasm (skin and systemic [malignant, uncertain behavior, benign])	EXC	18	17	13	18	18	17
Participants with a Prostatectomy or Radiation Treatment on the Prostate Gland	EXC	63	85	36	63	63	85

[a]777 Ranch Hands and 1,174 Comparisons for group.
[b]424 Ranch Hands for initial dioxin; 776 Ranch Hands for 1987 dioxin.
[c]776 Ranch Hands and 1,174 Comparisons for categorized dioxin.

Note: COV = Covariate.
        EXC = Exclusion.

10.2   RESULTS

10.2.1   Dependent Variable-covariate Associations

The neoplasia dependent variables were tested for associations with each of the covariates used in the adjusted analyses. The complete results are presented in Appendix F, Table F-2. These associations were pairwise between the dependent variable and the covariate and were not adjusted for any other covariates.

A brief summary of the pattern of significant ($p \leq 0.05$) dependent variable-covariate associations is described in the following paragraphs.

Older participants were more likely than younger participants to have developed a skin neoplasm, a malignant skin neoplasm, a benign skin neoplasm, basal cell carcinoma, squamous cell carcinoma, nonmelanoma, and melanoma. The prevalence of a systemic neoplasm, a malignant systemic neoplasm, a benign systemic neoplasm, a skin or systemic neoplasm, and a malignant skin or systemic neoplasm also was greater for older participants than for younger participants. Neoplasms of the bronchus or lung, urinary system, prostate, and other neoplasms of lymphoid or histiocytic tissue were also more common in older participants than younger participants. PSA levels increased with increasing age, and abnormally high levels of PSA were more likely to be seen in older participants.

Black participants were significantly less likely to develop a skin or systemic neoplasm and a malignant skin or systemic neoplasm than non-Black participants.

Officers were more likely than enlisted personnel to have any skin neoplasm, a malignant skin neoplasm, basal cell carcinoma, squamous cell carcinoma, and nonmelanoma. In addition, officers were more likely to have developed any systemic neoplasm and a lymphoreticular sarcoma than enlisted personnel. Officers also had a higher frequency of any skin or systemic neoplasm and any malignant skin or systemic neoplasm than enlisted personnel. Abnormally high PSA levels were more frequent in officers than enlisted personnel. A malignant systemic neoplasm, a malignant systemic neoplasm of the prostate, a malignant systemic neoplasm of the penis or other male genital organs, and carcinoma in situ had a higher prevalence in enlisted flyers than in officers or enlisted groundcrew. Mean PSA levels were highest in enlisted flyers, followed by officers, then enlisted groundcrew. For all of these dependent variables, enlisted groundcrew had the lowest prevalence, and presumably many of the associations seen here were at least partially due to age. On average, officers were older than enlisted personnel.

PSA levels decreased with increasing body mass index.

Participants exposed to ionizing radiation were more likely to have developed malignant systemic neoplasms and malignant systemic neoplasms of the oral cavity, pharynx, or larynx and urinary system than participants who were not exposed.

Participants with peach skin color were more likely than participants with nonpeach skin color to develop a skin neoplasm, a malignant skin neoplasm, a benign skin neoplasm, a skin or systemic neoplasm, a malignant skin or systemic neoplasm, squamous cell carcinoma, and nonmelanoma.

Malignant skin neoplasms, basal cell carcinoma, squamous cell carcinoma, nonmelanoma, a skin or systemic neoplasm, and a malignant skin or systemic neoplasm were less prevalent in participants with black or dark-brown hair than in participants with lighter-colored hair.

Participants with gray or blue eyes were more likely to have a skin neoplasm, a malignant skin neoplasm, nonmelanoma, melanoma, and a malignant skin or systemic neoplasm than participants with hazel, green, or brown eyes. Skin neoplasms of an uncertain behavior or an unspecified nature, basal cell carcinoma, and a skin or systemic neoplasm were more prevalent in participants with green or hazel eyes than in participants with gray, blue, or brown eyes.

The prevalence of a malignant skin neoplasm, basal cell carcinoma, squamous cell carcinoma, nonmelanoma, melanoma, and a malignant skin or systemic neoplasm increased as the severity of the skin reaction to sun after first exposure increased.

Participants who freckle after repeated exposure to the sun were significantly more likely to have had a skin neoplasm, a malignant skin neoplasm, basal cell carcinoma, squamous cell carcinoma, nonmelanoma, a skin or systemic neoplasm, and a malignant skin or systemic neoplasm than those who tan with repeated exposure to the sun. Participants who tan mildly after repeated sun exposure were more likely to develop melanoma than other participants.

The prevalence of a skin neoplasm, a malignant skin neoplasm, basal cell carcinoma, squamous cell carcinoma, nonmelanoma, a skin or systemic neoplasm, and a malignant skin or systemic neoplasm increased as the reaction to sun became more severe.

Participants with an average lifetime residential history closer to the equator had a greater prevalence of a malignant skin neoplasm, basal cell carcinoma, squamous cell carcinoma, nonmelanoma, and a malignant skin or systemic neoplasm than participants living further from the equator.

Cumulative industrial chemical exposure was not significantly associated with dependent variables for neoplasia.

A malignant systemic neoplasm of the bronchus or lung, a skin or systemic neoplasm, and a malignant skin or systemic neoplasm were more likely to be seen in participants with herbicide exposure than participants who were not exposed.

The heaviest lifetime cigarette smokers (>10 pack-years) were more likely to have developed a malignant systemic neoplasm, a malignant systemic neoplasm of the bronchus or lung, and a malignant skin or systemic neoplasm.

Nondrinkers were more likely to have a malignant systemic neoplasm of the urinary system and a malignant systemic neoplasm of the penis or other male genital organs than moderate or heavy drinkers.

10.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 10-1. Dependent variables are grouped into two sections: (1) variables derived from the questionnaire that was administered during the 2002 follow-up and previous AFHS examinations and subsequently verified by a review of medical records, and (2) PSA, as obtained during the 2002 laboratory examination.

10.2.2.1   Medical Records Variables

10.2.2.1.1 All Skin Neoplasms

Significant group differences were found when combining all occupations in both the unadjusted and adjusted analyses of Model 1 for occurrence of skin neoplasms (Table 10-3(a,b): Unadjusted Relative Risk [RR]=1.29, $p=0.007$; Adjusted RR=1.28, $p=0.012$). The percentage of Ranch Hands with skin neoplasms was 54.2 percent versus 47.8 percent for Comparisons. Results were nonsignificant for all other Model 1 analyses (Table 10-3(a,b): $p> 0.05$ for all analyses).

Results from the unadjusted Model 2 analysis indicated a significant inverse relation between initial dioxin and occurrence of skin neoplasms (Table 10-3(c): Adjusted RR=0.82, $p=0.011$). After adjusting for covariates, the results were not significant (Table 10-3(d): $p=0.313$).

The percentages of Ranch Hands with a skin neoplasm in the background dioxin category, the low dioxin category, and the low and high dioxin categories combined were all found to be significantly higher than the percentage of Comparisons with skin neoplasms (Table 10-3(e): Unadjusted RR=1.31, p=0.035 for Ranch Hands in the background dioxin category; Unadjusted RR=1.69, p=0.001 for Ranch Hands in the low dioxin category; Unadjusted RR=1.28, p=0.037 for Ranch Hands in the low and high dioxin categories combined).

After adjusting for covariates, significant differences were found when contrasting the Ranch Hands in both the low dioxin category and low and high dioxin categories combined with Comparisons (Table 10-3(f): Adjusted RR=1.56, p=0.007 for Ranch Hands in the low dioxin category; Adjusted RR=1.32, p=0.026 for Ranch Hands in the low and high dioxin categories combined). The percentages of participants with skin neoplasms were 61.0 and 54.2 for Ranch Hands in the low dioxin category and the low and high dioxin categories combined, respectively. The percentage of Comparisons with skin neoplasms was 47.8. All other Model 3 contrasts were nonsignificant (Table 10-3(e,f): p>0.10 for all analyses).

The Model 4 unadjusted and adjusted analyses did not reveal significant findings (Table 10-3(g,h): p>0.55 for both analyses).

Table 10-3. Analysis of All Skin Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*721*	*391 (54.2)*	*1.29 (1.07,1.56)*	*0.007** *
	Comparison	*1,086*	*519 (47.8)*		
Officer	Ranch Hand	296	172 (58.1)	1.34 (1.00,1.80)	0.054
	Comparison	448	228 (50.9)		
Enlisted Flyer	Ranch Hand	123	70 (56.9)	1.29 (0.81,2.06)	0.285
	Comparison	170	86 (50.6)		
Enlisted Groundcrew	Ranch Hand	302	149 (49.3)	1.25 (0.93,1.67)	0.133
	Comparison	468	205 (43.8)		

**: Statistically significant (p-value≤0.010).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,800*	*1.28 (1.06,1.56)*	*0.012**
Officer	740	1.32 (0.98,1.79)	0.069
Enlisted Flyer	293	1.23 (0.76,1.98)	0.400
Enlisted Groundcrew	767	1.26 (0.94,1.70)	0.122

*: Statistically significant (0.010<p-value≤0.050).

Table 10-3. Analysis of All Skin Neoplasms (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	123	80 (65.0)	0.82 (0.71,0.96)	0.011*
Medium	132	72 (54.5)		
High	134	59 (44.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
389	0.91 (0.75,1.10)	0.313

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,086	519 (47.8)		
Background RH	331	179 (54.1)	1.31 (1.02,1.67)	0.035*
Low RH	187	114 (61.0)	1.69 (1.23,2.32)	0.001**
High RH	202	97 (48.0)	0.99 (0.73,1.34)	0.965
Low plus High RH	389	211 (54.2)	1.28 (1.01,1.62)	0.037*

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-3. Analysis of All Skin Neoplasms (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,081		
Background RH	329	1.24 (0.96,1.60)	0.107
Low RH	187	1.56 (1.13,2.17)	0.007**
High RH	202	1.13 (0.82,1.55)	0.465
Low plus High RH	389	1.32 (1.03,1.68)	0.026*

[a]Relative risk and confidence interval relative to Comparisons.

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	246	126 (51.2)	0.97 (0.89,1.07)	0.559
Medium	233	147 (63.1)		
High	241	117 (48.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
718	1.00 (0.89,1.12)	0.968

[a]Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.2 Malignant Skin Neoplasms

All unadjusted and adjusted analyses of malignant skin neoplasms were nonsignificant for Model 1 (Table 10-4(a,b): p>0.05 for all analyses).

A significant inverse relation between initial dioxin levels and the occurrence of malignant skin neoplasms was revealed in the Model 2 unadjusted analysis (Table 10-4(c): Unadjusted RR=0.81, p=0.021). Results were nonsignificant after adjusting for covariates (Table 10-4(d): p=0.693).

The Model 3 unadjusted analysis showed significantly more Ranch Hands in the low dioxin category with malignant skin neoplasms than Comparisons (Table 10-4(e): Unadjusted RR=1.66, p=0.004). Of the Ranch Hands in the low dioxin category, 31.6 percent had malignant skin neoplasms versus 21.5 percent of the Comparisons. The result was also significant after adjusting for covariates (Table 10-4(f): Adjusted RR=1.52, p=0.024). All other Model 3 contrasts were nonsignificant (Table 10-4(e,f): p>0.07 for all analyses).

Both the unadjusted and adjusted Model 4 analyses were nonsignificant (Table 10-4(g,h): p>0.26 for both analyses).

Table 10-4. Analysis of Malignant Skin Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*721*	*183 (25.4)*	*1.24 (0.99,1.55)*	*0.059*
	Comparison	*1,086*	*234 (21.5)*		
Officer	Ranch Hand	296	94 (31.8)	1.36 (0.99,1.89)	0.061
	Comparison	448	114 (25.4)		
Enlisted Flyer	Ranch Hand	123	36 (29.3)	1.44 (0.85,2.44)	0.180
	Comparison	170	38 (22.4)		
Enlisted Groundcrew	Ranch Hand	302	53 (17.5)	1.00 (0.68,1.47)	0.992
	Comparison	468	82 (17.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,800*	*1.23 (0.97,1.55)*	*0.089*
Officer	740	1.33 (0.95,1.87)	0.100
Enlisted Flyer	293	1.40 (0.80,2.44)	0.235
Enlisted Groundcrew	767	1.03 (0.69,1.53)	0.889

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	123	38 (30.9)	0.81 (0.68,0.97)	0.021*
Medium	132	35 (26.5)		
High	134	23 (17.2)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 10-4. Analysis of Malignant Skin Neoplasms (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
389	0.96 (0.76,1.20)	0.693

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,086	234 (21.5)		
Background RH	331	86 (26.0)	1.30 (0.98,1.73)	0.073
Low RH	187	59 (31.6)	1.66 (1.18,2.34)	0.004**
High RH	202	37 (18.3)	0.80 (0.54,1.18)	0.261
Low plus High RH	389	96 (24.7)	1.14 (0.86,1.50)	0.365

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,081		
Background RH	329	1.15 (0.84,1.56)	0.378
Low RH	187	1.52 (1.06,2.19)	0.024*
High RH	202	1.06 (0.69,1.60)	0.801
Low plus High RH	389	1.26 (0.93,1.70)	0.134

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-4. Analysis of Malignant Skin Neoplasms (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	246	61 (24.8)	0.94 (0.85,1.05)	0.261
Medium	233	68 (29.2)		
High	241	53 (22.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
718	1.06 (0.92,1.22)	0.425

[a]Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.3 Benign Skin Neoplasms

All unadjusted and adjusted analyses of benign skin neoplasms were nonsignificant for Models 1 through 4 (Table 10-5(a-h): p>0.06 for all analyses).

Table 10-5. Analysis of Benign Skin Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*295 (38.3)*	*1.20 (0.99,1.44)*	*0.065*
	Comparison	*1,161*	*397 (34.2)*		
Officer	Ranch Hand	303	117 (38.6)	1.18 (0.87,1.60)	0.276
	Comparison	455	158 (34.7)		
Enlisted Flyer	Ranch Hand	132	51 (38.6)	1.14 (0.72,1.82)	0.572
	Comparison	183	65 (35.5)		
Enlisted Groundcrew	Ranch Hand	335	127 (37.9)	1.22 (0.92,1.63)	0.165
	Comparison	523	174 (33.3)		

Table 10-5. Analysis of Benign Skin Neoplasms (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,924*	*1.19 (0.98,1.44)*	*0.079*
Officer	754	1.21 (0.89,1.65)	0.213
Enlisted Flyer	315	1.10 (0.69,1.76)	0.697
Enlisted Groundcrew	855	1.20 (0.90,1.61)	0.214

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	137	62 (45.3)	0.89 (0.77,1.04)	0.147
Medium	142	52 (36.6)		
High	141	46 (32.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
420	0.91 (0.76,1.09)	0.296

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,161	397 (34.2)		
Background RH	349	135 (38.7)	1.23 (0.96,1.58)	0.103
Low RH	208	84 (40.4)	1.30 (0.96,1.76)	0.090
High RH	212	76 (35.8)	1.06 (0.78,1.44)	0.699
Low plus High RH	420	160 (38.1)	1.17 (0.93,1.48)	0.177

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　 Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
　　　 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
　　　 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-5. Analysis of Benign Skin Neoplasms (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,156		
Background RH	347	1.25 (0.97,1.61)	0.091
Low RH	208	1.25 (0.92,1.70)	0.155
High RH	212	1.05 (0.76,1.44)	0.780
Low plus High RH	420	1.14 (0.90,1.45)	0.272

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	258	96 (37.2)	0.98 (0.90,1.07)	0.686
Medium	254	113 (44.5)		
High	257	86 (33.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
767	0.96 (0.86,1.07)	0.469

[a]Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.4 Skin Neoplasms of Uncertain Behavior or Unspecified Nature

A sparse number of participants exhibited skin neoplasms of uncertain behavior or unspecified nature and thus analyses were limited. All analyzed results from the Model 1 and Model 4 unadjusted and adjusted analyses of skin neoplasms of uncertain behavior or unspecified nature were nonsignificant (Table 10-6(a,b,g,h): p≥0.10 for all analyses).

The unadjusted analysis of Model 2 revealed a significant inverse relation between initial dioxin and the occurrence of skin neoplasms of uncertain behavior or unspecified nature (Table 10-6(c): Unadjusted RR=0.25, p=0.018). The relation remained significant after adjusting for covariates (Table 10-6(d):

Adjusted RR=0.23, p=0.033). Of the Ranch Hands in the low and medium initial dioxin categories, 2.4 percent and 0.8 percent, respectively, had skin neoplasms of uncertain behavior or unspecified nature. There were no Ranch Hands in the high initial dioxin category with skin neoplasms of uncertain behavior or unspecified nature.

In both the Model 3 unadjusted and adjusted analyses, Ranch Hands in the low dioxin category had a significantly higher occurrence of skin neoplasms of uncertain behavior or unspecified nature than Comparisons (Table 10-6(e,f): Unadjusted RR=4.51, p=0.026; Adjusted RR=4.14, p=0.041, respectively). For Ranch Hands in the low dioxin category, 2.1 percent had skin neoplasms of uncertain behavior or unspecified nature versus 0.5 percent for Comparisons.

Table 10-6. Analysis of Skin Neoplasms of Uncertain Behavior or Unspecified Nature

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*721*	*8 (1.1)*	*2.43 (0.79,7.44)*	*0.115*
	Comparison	*1,086*	*5 (0.5)*		
Officer	Ranch Hand	296	5 (1.7)	2.55 (0.60,10.75)	0.203
	Comparison	448	3 (0.7)		
Enlisted Flyer	Ranch Hand	123	0 (0.0)	--	--
	Comparison	170	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	302	3 (1.0)	2.34 (0.39,14.07)	0.354
	Comparison	468	2 (0.4)		

--: Results were not presented because of the sparse number of participants with a skin neoplasm of uncertain behavior or unspecified nature.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,800*	*2.55 (0.82,7.97)*	*0.100*
Officer	740	2.68 (0.63,11.50)	0.184
Enlisted Flyer	293	--	--
Enlisted Groundcrew	767	2.41 (0.39,14.92)	0.344

--: Results were not presented because of the sparse number of participants with a skin neoplasm of uncertain behavior or unspecified nature.

Note: Results were not adjusted for military occupation, eye color, skin reaction to sun after first exposure, and skin reaction to sun after repeated exposure because of the sparse number of participants with a skin neoplasm of uncertain behavior or unspecified nature.

Table 10-6. Analysis of Skin Neoplasms of Uncertain Behavior or Unspecified Nature (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Yes**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	123	3 (2.4)	0.25 (0.05,1.16)	0.018*
Medium	132	1 (0.8)		
High	134	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
389	0.23 (0.04,1.38)	0.033*

[a]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: Results were not adjusted for military occupation, eye color, skin reaction to sun after first exposure, skin reaction to sun after repeated exposure, the composite skin-reaction index, and average lifetime residential latitude because of the sparse number of Ranch Hands with a skin neoplasm of uncertain behavior or unspecified nature.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,086	5 (0.5)		
Background RH	331	4 (1.2)	2.83 (0.75,10.71)	0.125
Low RH	187	4 (2.1)	4.51 (1.19,17.06)	0.026*
High RH	202	0 (0.0)	--	0.726[c]
Low plus High RH	389	4 (1.0)	--	0.393[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of
   participants with a skin neoplasm of uncertain behavior or unspecified nature.

*: Statistically significant (0.010<p-value≤0.050).

--: Results were not presented because of the sparse number of participants with a skin neoplasm of uncertain
     behavior or unspecified nature.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,081		
Background RH	329	2.60 (0.68,9.91)	0.162
Low RH	187	4.14 (1.06,16.16)	0.041*
High RH	202	--	--
Low plus High RH	389	--	--

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

--: Results were not presented because of the sparse number of participants with a skin neoplasm of uncertain
     behavior or unspecified nature.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

       Results were not adjusted for military occupation, eye color, skin reaction to sun after first exposure, and skin
       reaction to sun after repeated exposure because of the sparse number of participants with a skin neoplasm of
       uncertain behavior or unspecified nature.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	246	2 (0.8)	0.87 (0.56,1.35)	0.531
Medium	233	5 (2.1)		
High	241	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
718	0.84 (0.50,1.41)	0.509

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for military occupation, eye color, skin reaction to sun after first exposure, skin reaction to sun after repeated exposure, and the composite skin-reaction index because of the sparse number of Ranch Hands with a skin neoplasm of uncertain behavior or unspecified nature.

10.2.2.1.5 Basal Cell Carcinoma

The unadjusted Model 1 analysis revealed significant differences in the occurrence of basal cell carcinoma across all occupations and for officers (Table 10-7(a): Unadjusted RR=1.34, p=0.017 overall; Unadjusted RR=1.62, p=0.006 for officers). After covariate adjustment, both results remained significant (Table 10-7(b): Adjusted RR=1.33, p=0.027 overall; Adjusted RR=1.58, p=0.013 for officers). In the overall analysis, 21.4 percent of Ranch Hands had a history of basal cell carcinoma versus 16.9 percent of Comparisons. The percentage of Ranch Hand officers with basal cell carcinoma was 28.0 versus 19.4 percent for Comparison officers. All other Model 1 contrasts were nonsignificant (Table 10-7(a,b): p>0.21 for all analyses).

An inverse association between initial dioxin and occurrence of basal cell carcinoma was significant in the unadjusted Model 2 analysis (Table 10-7(c): Unadjusted RR=0.72, p=0.001). After covariate adjustment, the result was no longer significant (Table 10-7(d): p=0.309).

In the unadjusted Model 3 analyses, Ranch Hands in the background and low dioxin categories exhibited a higher occurrence of basal cell carcinoma than did Comparisons (Table 10-7(e): Unadjusted RR=1.47, p=0.012 for the background dioxin category; Unadjusted RR=1.78, p=0.002 for the low dioxin category). After covariate adjustment, the only significant difference occurred among those participants in the low dioxin category (Table 10-7(f): Adjusted RR=1.66, p=0.010). The percentages of participants with a basal cell carcinoma were 22.7 and 26.7 for Ranch Hands in the background and low dioxin categories, respectively. Among Comparisons, 16.9 percent exhibited a basal cell carcinoma.

The Model 4 unadjusted and adjusted analyses did not reveal any significant findings (Table 10-7(g,h): p>0.05 for both analyses).

Table 10-7. Analysis of Basal Cell Carcinoma

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*721*	*154 (21.4)*	*1.34 (1.06,1.70)*	*0.017**
	Comparison	*1,086*	*183 (16.9)*		
Officer	Ranch Hand	296	83 (28.0)	1.62 (1.14,2.28)	0.006**
	Comparison	448	87 (19.4)		
Enlisted Flyer	Ranch Hand	123	29 (23.6)	1.44 (0.81,2.55)	0.213
	Comparison	170	30 (17.6)		
Enlisted Groundcrew	Ranch Hand	302	42 (13.9)	0.98 (0.65,1.49)	0.939
	Comparison	468	66 (14.1)		

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,800*	*1.33 (1.03,1.71)*	*0.027**
Officer	740	1.58 (1.10,2.27)	0.013*
Enlisted Flyer	293	1.39 (0.76,2.51)	0.284
Enlisted Groundcrew	767	1.02 (0.66,1.57)	0.936

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	123	33 (26.8)	0.72 (0.59,0.89)	0.001**
Medium	132	30 (22.7)		
High	134	15 (11.2)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 10-7. Analysis of Basal Cell Carcinoma (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
389	0.88 (0.68,1.13)	0.309

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,086	183 (16.9)		
Background RH	331	75 (22.7)	1.47 (1.09,2.00)	0.012*
Low RH	187	50 (26.7)	1.78 (1.24,2.56)	0.002**
High RH	202	28 (13.9)	0.78 (0.50,1.20)	0.250
Low plus High RH	389	78 (20.1)	1.16 (0.85,1.57)	0.349

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,081		
Background RH	329	1.32 (0.95,1.82)	0.098
Low RH	187	1.66 (1.13,2.43)	0.010**
High RH	202	1.00 (0.63,1.58)	0.990
Low plus High RH	389	1.27 (0.92,1.76)	0.145

[a]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-7. Analysis of Basal Cell Carcinoma (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)**[a]	**p-Value**
Low	246	54 (22.0)	0.89 (0.80,1.00)	0.051
Medium	233	59 (25.3)		
High	241	40 (16.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk** **(95% C.I.)**[a]	**p-Value**
718	0.99 (0.85,1.15)	0.897

[a]Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.6 Squamous Cell Carcinoma

All results were nonsignificant in the Model 1 through 4 unadjusted and adjusted analyses of squamous cell carcinoma (Table 10-8(a-h): p>0.20 for all analyses).

Table 10-8. Analysis of Squamous Cell Carcinoma

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*721*	*45 (6.2)*	*1.12 (0.75,1.66)*	*0.581*
	Comparison	*1,086*	*61 (5.6)*		
Officer	Ranch Hand	296	24 (8.1)	1.01 (0.59,1.73)	0.972
	Comparison	448	36 (8.0)		
Enlisted Flyer	Ranch Hand	123	9 (7.3)	1.60 (0.60,4.27)	0.349
	Comparison	170	8 (4.7)		
Enlisted Groundcrew	Ranch Hand	302	12 (4.0)	1.10 (0.52,2.33)	0.808
	Comparison	468	17 (3.6)		

Table 10-8. Analysis of Squamous Cell Carcinoma (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,800*	*1.08 (0.71,1.63)*	*0.728*
Officer	740	0.97 (0.55,1.70)	0.916
Enlisted Flyer	293	1.53 (0.55,4.24)	0.417
Enlisted Groundcrew	767	1.08 (0.50,2.34)	0.847

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	123	9 (7.3)	0.82 (0.59,1.15)	0.246
Medium	132	10 (7.6)		
High	134	5 (3.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
389	0.96 (0.63,1.46)	0.861

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,086	61 (5.6)		
Background RH	331	20 (6.0)	1.09 (0.65,1.84)	0.750
Low RH	187	15 (8.0)	1.46 (0.81,2.63)	0.208
High RH	202	9 (4.5)	0.78 (0.38,1.59)	0.492
Low plus High RH	389	24 (6.2)	1.05 (0.64,1.74)	0.844

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-8. Analysis of Squamous Cell Carcinoma (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,081		
Background RH	329	0.91 (0.52,1.58)	0.728
Low RH	187	1.25 (0.67,2.33)	0.480
High RH	202	1.14 (0.52,2.49)	0.741
Low plus High RH	389	1.19 (0.69,2.05)	0.524

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	246	14 (5.7)	0.99 (0.82,1.20)	0.928
Medium	233	15 (6.4)		
High	241	15 (6.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
718	1.16 (0.90,1.50)	0.258

[a]Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.7 Nonmelanoma

The unadjusted Model 1 analyses of nonmelanoma revealed a significant overall difference between Ranch Hands and Comparisons, as well as a significant difference between Ranch Hand and Comparison officers (Table 10-9(a): Unadjusted RR=1.31, p=0.019 overall; Unadjusted RR=1.49, p=0.019 for officers). After covariate adjustment, both results remained significant (Table 10-9(b): Adjusted RR=1.31, p=0.027 overall; Adjusted RR=1.46, p=0.032 for officers). Occurrence of nonmelanoma was higher in Ranch Hands than in Comparisons (24.3% versus 19.6% overall, and 30.7% versus 23.0% among officers). All other Model 1 contrasts were nonsignificant (Table 10-9(a,b): p>0.08 for all analyses).

The Model 2 unadjusted analysis revealed a significant inverse association between initial dioxin and occurrence of nonmelanoma (Table 10-9(c): Unadjusted RR=0.77, p=0.005). After adjusting for covariates, the association was nonsignificant (Table 10-9(d): p=0.484).

The Model 3 unadjusted analysis revealed that Ranch Hands in the background dioxin category and the low dioxin category each had higher occurrences of nonmelanoma than Comparisons (Table 10-9(e): Unadjusted RR=1.42, p=0.018 for the background dioxin category; Unadjusted RR=1.73, p=0.002 for the low dioxin category). After adjusting for covariates, the only significant result occurred among the Ranch Hands in the low dioxin category (Table 10-9(f): Adjusted RR=1.60, p=0.013). The percentages of participants with nonmelanoma were 29.9 and 19.6 among Ranch Hands in the low dioxin category and Comparisons, respectively.

All results in the Model 4 unadjusted and adjusted analyses were nonsignificant (Table 10-9(g,h): p>0.11 for both analyses).

Table 10-9. Analysis of Nonmelanoma

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*721*	*175 (24.3)*	*1.31 (1.05,1.65)*	*0.019**
	Comparison	*1,086*	*213 (19.6)*		
Officer	Ranch Hand	296	91 (30.7)	1.49 (1.07,2.07)	0.019*
	Comparison	448	103 (23.0)		
Enlisted Flyer	Ranch Hand	123	36 (29.3)	1.60 (0.93,2.73)	0.088
	Comparison	170	35 (20.6)		
Enlisted Groundcrew	Ranch Hand	302	48 (15.9)	0.99 (0.67,1.47)	0.961
	Comparison	468	75 (16.0)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,800*	*1.31 (1.03,1.67)*	*0.027**
Officer	740	1.46 (1.03,2.07)	0.032*
Enlisted Flyer	293	1.58 (0.90,2.78)	0.110
Enlisted Groundcrew	767	1.02 (0.68,1.55)	0.907

*: Statistically significant (0.010<p-value≤0.050).

Table 10-9. Analysis of Nonmelanoma (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Yes**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	123	37 (30.1)	0.77 (0.64,0.93)	0.005**
Medium	132	33 (25.0)		
High	134	20 (14.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
389	0.92 (0.73,1.16)	0.484

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,086	213 (19.6)		
Background RH	331	84 (25.4)	1.42 (1.06,1.90)	0.018*
Low RH	187	56 (29.9)	1.73 (1.22,2.45)	0.002**
High RH	202	34 (16.8)	0.81 (0.54,1.21)	0.306
Low plus High RH	389	90 (23.1)	1.17 (0.88,1.56)	0.287

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-9. Analysis of Nonmelanoma (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,081		
Background RH	329	1.28 (0.94,1.74)	0.124
Low RH	187	1.60 (1.10,2.31)	0.013*
High RH	202	1.06 (0.69,1.64)	0.783
Low plus High RH	389	1.29 (0.95,1.76)	0.102

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.010 < $p-value$\leq 0.050$).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	246	60 (24.4)	0.92 (0.83,1.02)	0.118
Medium	233	66 (28.3)		
High	241	48 (19.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
718	1.02 (0.88,1.18)	0.789

[a]Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.8 Melanoma

All unadjusted and adjusted analyses of melanoma in Models 1 through 4 were nonsignificant (Table 10-10(a-h): p>0.07 for all analyses).

Table 10-10. Analysis of Melanoma

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*721*	*19 (2.6)*	*0.92 (0.52,1.64)*	*0.780*
	Comparison	*1,086*	*31 (2.9)*		
Officer	Ranch Hand	296	11 (3.7)	0.98 (0.45,2.12)	0.956
	Comparison	448	17 (3.8)		
Enlisted Flyer	Ranch Hand	123	1 (0.8)	0.27 (0.03,2.34)	0.235
	Comparison	170	5 (2.9)		
Enlisted Groundcrew	Ranch Hand	302	7 (2.3)	1.21 (0.45,3.28)	0.708
	Comparison	468	9 (1.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,800*	*0.93 (0.52,1.68)*	*0.813*
Officer	740	1.03 (0.47,2.27)	0.937
Enlisted Flyer	293	0.25 (0.03,2.19)	0.210
Enlisted Groundcrew	767	1.18 (0.43,3.23)	0.755

Note: Results were not adjusted for skin reaction to sun after first exposure because of the sparse number of participants with melanoma.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	123	5 (4.1)	0.99 (0.63,1.55)	0.968
Medium	132	2 (1.5)		
High	134	4 (3.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 10-10. Analysis of Melanoma (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (Initial Dioxin) | |
| | Adjusted Relative Risk | |
n	(95% C.I.)[a]	p-Value
389	1.07 (0.66,1.74)	0.788

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for military occupation, skin reaction to sun after first exposure, and skin reaction to sun after repeated exposure because of the sparse number of Ranch Hands with melanoma.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,086	31 (2.9)		
Background RH	331	8 (2.4)	0.85 (0.38,1.87)	0.682
Low RH	187	7 (3.7)	1.32 (0.57,3.04)	0.517
High RH	202	4 (2.0)	0.68 (0.24,1.96)	0.479
Low plus High RH	389	11 (2.8)	0.94 (0.45,1.94)	0.861

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,081		
Background RH	329	0.75 (0.33,1.68)	0.486
Low RH	187	1.23 (0.52,2.90)	0.642
High RH	202	1.01 (0.33,3.09)	0.980
Low plus High RH	389	1.11 (0.52,2.38)	0.786

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Note: Results were not adjusted for skin reaction to sun after first exposure because of the sparse number of participants with melanoma.

Table 10-10. Analysis of Melanoma (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Yes**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	246	5 (2.0)	1.07 (0.82,1.42)	0.611
Medium	233	8 (3.4)		
High	241	6 (2.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
718	1.44 (0.96,2.14)	0.071

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for skin reaction to sun after first exposure and skin reaction to sun after repeated exposure because of the sparse number of Ranch Hands with melanoma.

10.2.2.1.9 Systemic Neoplasms (All Sites Combined)

Results from the analyses of all systemic neoplasms in Models 1, 2, and 4, both unadjusted and adjusted, were nonsignificant (Table 10-11(a-d,g,h): p≥0.16 for all analyses).

In the unadjusted analyses for Model 3, a significant difference in the percentage of participants with a systemic neoplasm was found between Ranch Hands in the low dioxin category and Comparisons (Table 10-11(e): Unadjusted RR=1.39, p=0.033). After adjusting for covariates, the contrast was nonsignificant (Table 10-11(f): p=0.174). All other Model 3 contrasts were nonsignificant in both the unadjusted and adjusted analyses (Table 10-15(e,f): p>0.34 for all analyses).

Table 10-11. Analysis of Systemic Neoplasms (All Sites Combined)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*765*	*262 (34.2)*	*1.05 (0.86,1.27)*	*0.649*
	Comparison	*1,170*	*389 (33.2)*		
Officer	Ranch Hand	301	115 (38.2)	1.03 (0.76,1.39)	0.838
	Comparison	459	172 (37.5)		
Enlisted Flyer	Ranch Hand	129	48 (37.2)	1.18 (0.73,1.88)	0.500
	Comparison	185	62 (33.5)		
Enlisted Groundcrew	Ranch Hand	335	99 (29.6)	1.00 (0.74,1.36)	0.979
	Comparison	526	155 (29.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,925*	*1.01 (0.80,1.28)*	*0.939*
Officer	759	1.00 (0.72,1.39)	0.996
Enlisted Flyer	312	1.12 (0.68,1.84)	0.656
Enlisted Groundcrew	854	0.98 (0.70,1.37)	0.892

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	135	55 (40.7)	0.90 (0.77,1.05)	0.160
Medium	141	49 (34.8)		
High	138	44 (31.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
412	0.99 (0.82,1.20)	0.938

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,170	389 (33.2)		
Background RH	350	114 (32.6)	1.00 (0.77,1.29)	0.993
Low RH	204	84 (41.2)	1.39 (1.03,1.89)	0.033*
High RH	210	64 (30.5)	0.86 (0.62,1.18)	0.345
Low plus High RH	414	148 (35.7)	1.09 (0.86,1.38)	0.482

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,164		
Background RH	348	0.90 (0.67,1.20)	0.471
Low RH	203	1.27 (0.90,1.79)	0.174
High RH	209	1.00 (0.69,1.45)	0.999
Low plus High RH	412	1.12 (0.85,1.50)	0.418

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	87 (33.6)	0.98 (0.89,1.08)	0.689
Medium	252	92 (36.5)		
High	253	83 (32.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 10-11. Analysis of Systemic Neoplasms (All Sites Combined) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
760	1.05 (0.93,1.18)	0.434

[a]Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.10 Malignant Systemic Neoplasms (All Sites Combined)

The unadjusted Model 1 analyses revealed significantly more Ranch Hand officers than Comparison officers with a malignant systemic neoplasm (Table 10-12(a): Unadjusted RR=1.63, p=0.023). Among Ranch Hand officers, 16.6 percent exhibited a malignant systemic neoplasm, as compared to 10.8 percent among Comparison officers. After adjusting for covariates, the contrast remained significant (Table 10-12(b): Adjusted RR=1.81, p=0.014). All other Model 1 contrasts were nonsignificant (Table 10-12(a,b): p>0.05 for all analyses).

The unadjusted Model 2 analysis of malignant systemic neoplasms revealed a significant inverse relation with initial dioxin (Table 10-12(c): Unadjusted RR=0.69, p=0.001). The association was nonsignificant after adjusting for covariates (Table 10-12(d): p=0.898).

The Model 3 contrast between Ranch Hands in the low dioxin category and Comparisons was significant in both the unadjusted and adjusted analyses (Table 10-12(e,f): Unadjusted RR=2.15, p<0.001; Adjusted RR=2.05, p=0.003, respectively). A greater percentage of participants with malignant systemic neoplasms was observed in Ranch Hands than in Comparisons (19.4% versus 10.1%, respectively). All other Model 3 results were nonsignificant (Table 10-12(e,f): p>0.07 for all analyses).

There were no significant findings in the Model 4 unadjusted and adjusted analyses (Table 10-12(g,h): p>0.16 for both analyses).

Table 10-12. Analysis of Malignant Systemic Neoplasms (All Sites Combined)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*97 (12.6)*	*1.29 (0.97,1.72)*	*0.082*
	Comparison	*1,172*	*118 (10.1)*		
Officer	Ranch Hand	302	50 (16.6)	1.63 (1.07,2.49)	0.023*
	Comparison	461	50 (10.8)		
Enlisted Flyer	Ranch Hand	131	25 (19.1)	1.84 (0.98,3.46)	0.057
	Comparison	185	21 (11.4)		
Enlisted Groundcrew	Ranch Hand	336	22 (6.5)	0.71 (0.42,1.21)	0.209
	Comparison	526	47 (8.9)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*1.37 (0.96,1.96)*	*0.082*
Officer	762	1.81 (1.13,2.91)	0.014*
Enlisted Flyer	313	1.87 (0.94,3.71)	0.073
Enlisted Groundcrew	855	0.72 (0.40,1.30)	0.281

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	26 (19.1)	0.69 (0.54,0.88)	0.001**
Medium	142	21 (14.8)		
High	140	10 (7.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
415	0.98 (0.72,1.33)	0.898

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	118 (10.1)		
Background RH	350	40 (11.4)	1.16 (0.79,1.70)	0.444
Low RH	206	40 (19.4)	2.15 (1.45,3.19)	<0.001**
High RH	212	17 (8.0)	0.77 (0.45,1.32)	0.345
Low plus High RH	418	57 (13.6)	1.28 (0.89,1.83)	0.179

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	1.15 (0.74,1.80)	0.525
Low RH	205	2.05 (1.28,3.26)	0.003**
High RH	210	1.09 (0.59,2.01)	0.778
Low plus High RH	415	1.49 (0.96,2.30)	0.074

[a]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	31 (12.0)	0.91 (0.79,1.04)	0.166
Medium	253	42 (16.6)		
High	256	24 (9.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

*Table 10-12. Analysis of Malignant Systemic Neoplasms (All Sites Combined)
(Continued)*

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (1987 Dioxin) | |
| | **Adjusted Relative Risk** | |
n	**(95% C.I.)^a**	**p-Value**
763	1.00 (0.83,1.21)	0.963

^{a}Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.11   Benign Systemic Neoplasms (All Sites Combined)

Results from each of the unadjusted and adjusted analyses of benign systemic neoplasms in Models 1 through 4 were nonsignificant (Table 10-13(a-h): p>0.32 for all analyses).

Table 10-13. Analysis of Benign Systemic Neoplasms (All Sites Combined)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*765*	*192 (25.1)*	*1.00 (0.81,1.23)*	*0.988*
	Comparison	*1,170*	*294 (25.1)*		
Officer	Ranch Hand	301	80 (26.6)	0.89 (0.64,1.23)	0.472
	Comparison	459	133 (29.0)		
Enlisted Flyer	Ranch Hand	129	29 (22.5)	0.88 (0.52,1.49)	0.626
	Comparison	185	46 (24.9)		
Enlisted Groundcrew	Ranch Hand	335	83 (24.8)	1.18 (0.85,1.63)	0.322
	Comparison	526	115 (21.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,925*	*0.96 (0.74,1.23)*	*0.731*
Officer	759	0.85 (0.60,1.21)	0.368
Enlisted Flyer	312	0.84 (0.48,1.46)	0.528
Enlisted Groundcrew	854	1.14 (0.80,1.63)	0.474

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Yes**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	135	33 (24.4)	1.04 (0.88,1.23)	0.658
Medium	141	36 (25.5)		
High	138	36 (26.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
412	0.99 (0.81,1.22)	0.939

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,170	294 (25.1)		
Background RH	350	87 (24.9)	1.02 (0.77,1.34)	0.915
Low RH	204	53 (26.0)	1.04 (0.74,1.45)	0.842
High RH	210	52 (24.8)	0.96 (0.68,1.34)	0.793
Low plus High RH	414	105 (25.4)	0.99 (0.77,1.29)	0.963

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,164		
Background RH	348	0.92 (0.67,1.26)	0.605
Low RH	203	0.97 (0.67,1.41)	0.881
High RH	209	1.02 (0.69,1.51)	0.903
Low plus High RH	412	1.00 (0.74,1.35)	0.991

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	64 (24.7)	1.00 (0.91,1.11)	0.951
Medium	252	61 (24.2)		
High	253	67 (26.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
760	1.03 (0.91,1.16)	0.686

[a]Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.12   Systemic Neoplasms of Uncertain Behavior or Unspecified Nature (All Sites Combined)

Results from each of the unadjusted and adjusted analyses of systemic neoplasms of uncertain behavior or unspecified nature for Models 1 through 4 were nonsignificant (Table 10-14(a-h): p>0.20 for all analyses).

Table 10-14. Analysis of Systemic Neoplasms of Uncertain Behavior or Unspecified Nature (All Sites Combined)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*15 (2.0)*	*0.91 (0.48,1.74)*	*0.781*
	Comparison	*1,172*	*25 (2.1)*		
Officer	Ranch Hand	302	7 (2.3)	0.82 (0.32,2.07)	0.672
	Comparison	461	13 (2.8)		
Enlisted Flyer	Ranch Hand	131	3 (2.3)	2.14 (0.35,13.02)	0.407
	Comparison	185	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	336	5 (1.5)	0.78 (0.26,2.30)	0.652
	Comparison	526	10 (1.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*0.71 (0.34,1.49)*	*0.368*
Officer	762	0.66 (0.24,1.77)	0.407
Enlisted Flyer	313	1.61 (0.25,10.19)	0.613
Enlisted Groundcrew	855	0.59 (0.19,1.87)	0.372

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	3 (2.2)	0.95 (0.54,1.66)	0.845
Medium	142	2 (1.4)		
High	140	2 (1.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
415	1.13 (0.57,2.24)	0.736

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	25 (2.1)		
Background RH	350	8 (2.3)	1.14 (0.50,2.56)	0.757
Low RH	206	5 (2.4)	1.12 (0.42,2.95)	0.826
High RH	212	2 (0.9)	0.42 (0.10,1.77)	0.236
Low plus High RH	418	7 (1.7)	0.68 (0.27,1.70)	0.406

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	0.82 (0.34,1.99)	0.656
Low RH	205	0.83 (0.29,2.36)	0.726
High RH	210	0.37 (0.08,1.70)	0.201
Low plus High RH	415	0.55 (0.20,1.50)	0.243

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	7 (2.7)	0.94 (0.68,1.30)	0.722
Medium	253	4 (1.6)		
High	256	4 (1.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
763	0.97 (0.65,1.44)	0.880

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.13   Body Sites at Which a Sparse Number of Participants Had a Malignant Systemic Neoplasm

The analyses described below are based primarily on malignant systemic neoplasms by anatomical site. Analyses were attempted for a given site if the statistical software could compute the summary statistics without numerical complications. Analyses based on fewer than five cases in either group should be viewed with caution. Inferential statistics for such analyses (p-values and confidence intervals) should not be used in conclusions regarding herbicide or dioxin exposure and the risk of cancer.

Table 10-15 lists the sites with fewer than five cases of a malignant systemic neoplasm for either Ranch Hands or Comparisons. If analysis was attempted for neoplasms at that site, the table reference is given. If analysis was not attempted, "Not Analyzed" is given under the heading "Table Reference." Footnotes in the tables indicate where the analysis was limited or covariates were not included in the adjusted analysis due to small numbers of neoplasms, as adjustment for all covariates was often not possible.

Table 10-15. Body Sites at Which a Sparse Number of Participants Had a Malignant Systemic Neoplasm

		Number of Participants with a Neoplasm	
Site (ICD-9-CM Codes [with T Codes and M codes])	**Table Reference**	**Ranch Hand**	**Comparison**
Eye, Ear, Face, Head, and Neck (160.0 – 160.9, 170.0, 170.1, 171.0, 190.0 – 190.9, 195.0, 234.0, 234.8)	10-16	1	4
Oral Cavity, Pharynx, and Larynx (140.0 – 149.9, 161.0 – 161.9, 230.0, 231.0)	10-17	4	9
Thymus, Heart, and Mediastinum (164.0, 164.2 – 164.9, 197.1)	10-18	2	1
Thyroid Gland (193, 194.1)	10-19	1	2
Kidney and Ureter (189.0 – 189.2, 198.0, 233.9)	10-24	7	4
Penis and Other Male Genital Organs (187.2 – 187.6, 187.8, 187.9, 198.82)	10-26	2	0
Testicles (186.0, 186.9, 233.6)	10-27	3	0
Bone and Articular Cartilage (170.0 – 170.9, 198.5)	10-28	0	4
Connective and Other Soft Tissues (171.0 – 171.9)	10-29	1	6
Carcinoma In Situ (Breast, Digestive Organs, Respiratory, Prostate, Penis and Other Male Genitals, and Bladder and Other and Nonspecified Urinary) (230.0 – 231.9, 233.0, 233.4 – 234.9)	10-30	4	6

Site (ICD-9-CM Codes [with T Codes and M codes])	Table Reference	Number of Participants with a Neoplasm	
		Ranch Hand	Comparison
Hodgkin's Disease (201.00 – 201.98)	10-31	1	1
Leukemia (204.00 – 208.91)	10-32	4	6
Lymphoreticular Sarcoma (200.00 – 200.88)	10-34	1	3
Esophagus (150.0 – 150.9, 230.1)	Not Analyzed	0	2
Brain (191.0 – 191.9, 198.3)	Not Analyzed	0	1
Stomach (151.0 – 151.9, 230.2)	Not Analyzed	0	2
Liver (155.0 – 155.2, 197.7, 230.8)	Not Analyzed	0	1
Ill-defined Sites (195.1 – 195.8, 199.0, 199.1)	Not Analyzed	0	1
Lymphoma (202.00 – 202.08 [with any M code except M95913], 202.80 – 202.98)	Not Analyzed	0	2
Non-Hodgkin's Lymphoma (202.00 – 202.08) [M code M95913])	Not Analyzed	0	1
Multiple Myeloma (203.00, 203.11)	Not Analyzed	0	1

10.2.2.1.14   Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)

All unadjusted and adjusted analyses performed for malignant systemic neoplasms of the eye, ear, face, head, and neck from Models 1 through 4 were nonsignificant (Table 10-16(a-h): p>0.14 for all analyses).

Table 10-16. Analysis of Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*1 (0.1)*	*0.38 (0.04,3.41)*	*0.347*
	Comparison	*1,172*	*4 (0.3)*		
Officer	Ranch Hand	302	0 (0.0)	--	0.999[a]
	Comparison	461	1 (0.2)		
Enlisted Flyer	Ranch Hand	131	1 (0.8)	1.42 (0.09,22.84)	0.807
	Comparison	185	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	336	0 (0.0)	--	0.685[a]
	Comparison	526	2 (0.4)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the eye, ear, face, head, or neck.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the eye, ear, face, head, or neck.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)		p-Value
All	*1,930*	*0.30*	*(0.03,3.47)*	*0.316*
Officer	762	--		--
Enlisted Flyer	313	1.08	(0.05,21.84)	0.959
Enlisted Groundcrew	855	--		--

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the eye, ear, face, head, or neck.

Note: Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the eye, ear, face, head, or neck.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	0 (0.0)	2.50 (0.70,8.93)	0.159
Medium	142	0 (0.0)		
High	140	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	2.62 (0.67,10.23)	0.155

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for age, race, military occupation, cumulative ionizing radiation exposure, cumulative herbicide exposure, and lifetime alcohol history because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the eye, ear, face, head, or neck.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	4 (0.3)		
Background RH	350	0 (0.0)	--	0.617[c]
Low RH	206	0 (0.0)	--	0.891[c]
High RH	212	1 (0.5)	1.32 (0.14,12.02)	0.806
Low plus High RH	418	1 (0.2)	--	0.999[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of
 participants with a malignant systemic neoplasm of the eye, ear, face, head, or neck.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of
 the eye, ear, face, head, or neck.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	--	--
Low RH	205	--	--
High RH	210	0.99 (0.08,12.65)	0.991
Low plus High RH	415	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of
 the eye, ear, face, head, or neck.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

 Results were not adjusted for race because of the sparse number of participants with a malignant systemic
 neoplasm of the eye, ear, face, head, or neck.

Table 10-16. Analysis of Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
Low	259	0 (0.0)	2.35 (0.72,7.62)	0.144
Medium	253	0 (0.0)		
High	256	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
767	2.33 (0.74,7.37)	0.146

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for age, race, military occupation, cumulative ionizing radiation exposure, cumulative herbicide exposure, and lifetime alcohol history because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the eye, ear, face, head, or neck.

10.2.2.1.15 Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)

Results from each of the unadjusted and adjusted analyses performed for malignant systemic neoplasms of the oral cavity, pharynx, and larynx for Models 1, 3, and 4 were nonsignificant (Table 10-17(a,b,e-h): p>0.09 for all analyses).

The unadjusted analysis of Model 2 revealed a significant inverse relation between initial dioxin and occurrence of malignant systemic neoplasms of the oral cavity, pharynx, and larynx (Table 10-17(c): Unadjusted RR=0.21, p=0.017). The result remained significant after covariate adjustment (Table 10-17(d): Adjusted RR=0.12, p=0.010). Of the Ranch Hands in the low dioxin category, 2.9 percent had a malignant systemic neoplasm of the oral cavity, pharynx, or larynx, compared to none in the medium or high dioxin categories.

Table 10-17. Analysis of Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*4 (0.5)*	*0.68 (0.21,2.20)*	*0.506*
	Comparison	*1,172*	*9 (0.8)*		
Officer	Ranch Hand	302	1 (0.3)	0.51 (0.05,4.90)	0.557
	Comparison	461	3 (0.7)		
Enlisted Flyer	Ranch Hand	131	3 (2.3)	2.14 (0.35,13.02)	0.407
	Comparison	185	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	336	0 (0.0)	--	0.276[a]
	Comparison	526	4 (0.8)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the oral cavity, pharynx, or larynx.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the oral cavity, pharynx, or larynx.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*0.81 (0.20,3.25)*	*0.761*
Officer	762	0.76 (0.07,8.20)	0.823
Enlisted Flyer	313	2.69 (0.35,20.72)	0.341
Enlisted Groundcrew	855	--	--

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the oral cavity, pharynx, or larynx.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	4 (2.9)	0.21 (0.04,1.19)	0.017*
Medium	142	0 (0.0)		
High	140	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant ($0.010 < $ p-value ≤ 0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
415	0.12 (0.01,1.09)	0.010**

[a]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Results were not adjusted for race, military occupation, and cumulative herbicide exposure because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the oral cavity, pharynx, or larynx.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	9 (0.8)		
Background RH	350	0 (0.0)	--	0.212[c]
Low RH	206	4 (1.9)	2.62 (0.80,8.60)	0.112
High RH	212	0 (0.0)	--	0.415[c]
Low plus High RH	418	4 (1.0)	--	0.958[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the oral cavity, pharynx, or larynx.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the oral cavity, pharynx, or larynx.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	--	--
Low RH	205	3.69 (0.81,16.83)	0.092
High RH	210	--	--
Low plus High RH	415	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the oral cavity, pharynx, or larynx.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	0 (0.0)	1.04 (0.57,1.91)	0.889
Medium	253	4 (1.6)		
High	256	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	1.23 (0.64,2.38)	0.541

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, military occupation, and cumulative herbicide exposure because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the oral cavity, pharynx, or larynx.

10.2.2.1.16 Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)

The unadjusted and adjusted contrasts analyzed in Model 1 for malignant systemic neoplasms of the thymus, heart, and mediastinum were nonsignificant (Table 10-18(a,b): p>0.24 for both analyses).

Model 2 analysis was not performed because no Ranch Hands with an initial dioxin estimate had a malignant neoplasm of the thymus, heart, or mediastinum. The Model 3 unadjusted and adjusted analyses performed were nonsignificant (Table 10-18(e,f): p>0.12 for all analyses).

The Model 4 unadjusted and adjusted analyses showed a significant inverse association between 1987 dioxin levels and occurrence of malignant systemic neoplasms of the thymus, heart, and mediastinum (Table 10-18(g,h): Unadjusted RR=0.40; p=0.038; Adjusted RR=0.04, p=0.009, respectively). For Ranch Hands in the low 1987 dioxin category, 0.8 percent had a malignant systemic neoplasm of the thymus, heart and mediastinum, compared to no Ranch Hands in the medium or high dioxin categories.

Table 10-18. Analysis of Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*2 (0.3)*	*3.05 (0.28,33.73)*	*0.344*
	Comparison	*1,172*	*1 (0.1)*		
Officer	Ranch Hand	302	1 (0.3)	--	0.831[a]
	Comparison	461	0 (0.0)		
Enlisted Flyer	Ranch Hand	131	0 (0.0)	--	0.999[a]
	Comparison	185	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	336	1 (0.3)	--	0.821[a]
	Comparison	526	0 (0.0)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, or mediastinum.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, or mediastinum.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*7.34 (0.19,289.00)*	*0.247*
Officer	762	--	--
Enlisted Flyer	313	--	--
Enlisted Groundcrew	855	--	--

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, or mediastinum.

Note: Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, or mediastinum.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)**	**p-Value**
Low	136	0 (0.0)	--	--
Medium	142	0 (0.0)		
High	140	0 (0.0)		

--: Results were not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thymus, heart, or mediastinum.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk** **(95% C.I.)**	**p-Value**
415	--	--

--: Results were not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thymus, heart, or mediastinum.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	1 (0.1)		
Background RH	350	2 (0.6)	6.35 (0.56,72.10)	0.136
Low RH	206	0 (0.0)	--	0.999[c]
High RH	212	0 (0.0)	--	0.999[c]
Low plus High RH	418	0 (0.0)	--	0.999[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, or mediastinum.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, or mediastinum.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	17.36 (0.45,664.89)	0.125
Low RH	205	--	--
High RH	210	--	--
Low plus High RH	415	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, or mediastinum.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the thymus, heart, or mediastinum.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	2 (0.8)	0.40 (0.17,0.92)	0.038*
Medium	253	0 (0.0)		
High	256	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value$\leq$0.050).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

n	Analysis Results for Log$_2$ (1987 Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	0.04 (0.00,7.74)	0.009**

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Results were not adjusted for race, military occupation, or cumulative herbicide exposure because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thymus, heart, or mediastinum.

10.2.2.1.17 Malignant Systemic Neoplasms (Thyroid Gland)

For the unadjusted and adjusted analyses performed on malignant systemic neoplasms of the thyroid gland using Models 1 through 4, there were no significant results found (Table 10-19(a-h): p>0.19 for all analyses).

Table 10-19. Analysis of Malignant Systemic Neoplasms (Thyroid Gland)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*1 (0.1)*	*0.76 (0.07,8.42)*	*0.822*
	Comparison	*1,172*	*2 (0.2)*		
Officer	Ranch Hand	302	1 (0.3)	1.53 (0.10,24.53)	0.765
	Comparison	461	1 (0.2)		
Enlisted Flyer	Ranch Hand	131	0 (0.0)	--	--
	Comparison	185	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	336	0 (0.0)	--	0.999[a]
	Comparison	526	1 (0.2)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the thyroid gland.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the thyroid gland.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*0.70 (0.05,10.41)*	*0.794*
Officer	762	1.58 (0.08,33.16)	0.768
Enlisted Flyer	313	--	--
Enlisted Groundcrew	855	--	--

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the thyroid gland.

Note: Results were not adjusted for race, military occupation, and cumulative ionizing radiation exposure because of the sparse number of participants with a malignant systemic neoplasm of the thyroid gland.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	1 (0.7)	0.19 (0.01,6.58)	0.194
Medium	142	0 (0.0)		
High	140	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
415	0.19 (0.01,6.92)	0.218

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, cumulative ionizing radiation exposure, cumulative herbicide exposure, and lifetime cigarette smoking history because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thyroid gland.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	2 (0.2)		
Background RH	350	0 (0.0)	--	0.999[c]
Low RH	206	1 (0.5)	2.97 (0.27,33.03)	0.375
High RH	212	0 (0.0)	--	0.999[c]
Low plus High RH	418	1 (0.2)	--	0.999[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of
  participants with a malignant systemic neoplasm of the thyroid gland.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of
    the thyroid gland.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	--	--
Low RH	205	2.90 (0.18,47.88)	0.456
High RH	210	--	--
Low plus High RH	415	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of
    the thyroid gland.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

      Results were not adjusted for race, military occupation, and cumulative ionizing radiation exposure because
      of the sparse number of participants with a malignant systemic neoplasm of the thyroid gland.

Table 10-19. Analysis of Malignant Systemic Neoplasms (Thyroid Gland) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Yes**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	259	0 (0.0)	0.93 (0.27,3.22)	0.912
Medium	253	1 (0.4)		
High	256	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
763	0.85 (0.21,3.39)	0.817

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, military occupation, cumulative ionizing radiation exposure, cumulative herbicide exposure, and lifetime cigarette smoking history because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the thyroid gland.

10.2.2.1.18 Malignant Systemic Neoplasms (Bronchus and Lung)

The unadjusted Model 1 analyses of malignant systemic neoplasms of the bronchus and lung revealed a significant difference between Ranch Hands and Comparisons when examined across all occupations (Table 10-20(a): Unadjusted RR=2.86, p=0.021). The result was no longer significant after adjusting for covariates (Table 10-20(b): p=0.120). All other Model 1 contrasts were nonsignificant (Table 10-20(a,b): p≥0.10 for all analyses).

A significantly greater percentage of Ranch Hands in the low dioxin category (3.9%) had a malignant systemic neoplasm of the bronchus or lung than Comparisons (0.6%) in both the unadjusted and adjusted Model 3 analyses (Table 10-20(e,f): Unadjusted RR=6.43, p<0.001; Adjusted RR=3.91, p=0.024, respectively). Also in the unadjusted Model 3 analyses, a greater percentage of Ranch Hands in the low and high dioxin categories combined had a malignant systemic neoplasm of the bronchus or lung than Comparisons (Table 10-20(e): Unadjusted RR=3.01, p=0.047). The result was not significant after covariate adjustment (Table 10-20(f): p=0.162). All other Model 3 unadjusted and adjusted analyses were nonsignificant (Table 10-20(e,f): p≥0.50).

There were no significant findings in the Model 2 and Model 4 unadjusted and adjusted analyses of malignant systemic neoplasms of the bronchus and lung (Table 10-20(c,d,g,h): p>0.17 for all analyses).

Table 10-20. Analysis of Malignant Systemic Neoplasms (Bronchus and Lung)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*13 (1.7)*	*2.86 (1.14,7.21)*	*0.021**
	Comparison	*1,172*	*7 (0.6)*		
Officer	Ranch Hand	302	6 (2.0)	3.09 (0.77,12.47)	0.112
	Comparison	461	3 (0.7)		
Enlisted Flyer	Ranch Hand	131	3 (2.3)	1.42 (0.28,7.16)	0.669
	Comparison	185	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	336	4 (1.2)	6.33 (0.70,56.84)	0.100
	Comparison	526	1 (0.2)		

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*2.27 (0.78,6.62)*	*0.120*
Officer	762	2.63 (0.59,11.86)	0.207
Enlisted Flyer	313	1.14 (0.20,6.64)	0.882
Enlisted Groundcrew	855	4.39 (0.45,43.11)	0.205

Note: Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the bronchus or lung.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for $\mathrm{Log_2}$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	5 (3.7)	0.70 (0.40,1.22)	0.179
Medium	142	3 (2.1)		
High	140	2 (1.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 10-20. *Analysis of Malignant Systemic Neoplasms (Bronchus and Lung) (Continued)*

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
415	0.87 (0.44,1.71)	0.673

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the bronchus or lung. Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	7 (0.6)		
Background RH	350	3 (0.9)	1.60 (0.41,6.26)	0.500
Low RH	206	8 (3.9)	6.43 (2.30,18.02)	<0.001**
High RH	212	2 (0.9)	1.44 (0.30,7.04)	0.650
Low plus High RH	418	10 (2.4)	3.01 (1.02,8.95)	0.047*

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

 *: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).
**: Statistically significant ($\text{p-value} \leq 0.010$).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	1.30 (0.30,5.74)	0.728
Low RH	205	3.91 (1.20,12.74)	0.024*
High RH	210	1.52 (0.27,8.64)	0.636
Low plus High RH	415	2.42 (0.70,8.39)	0.162

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the bronchus or lung.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	2 (0.8)	1.10 (0.79,1.54)	0.567
Medium	253	6 (2.4)		
High	256	5 (2.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	1.21 (0.76,1.93)	0.411

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the bronchus or lung. Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.19 All Stomach Neoplasms

The unadjusted and adjusted analyses of Models 1 through 4 for stomach neoplasms (malignant and benign combined) did not reveal significant findings (Table 10-21(a-h): p>0.17 for all analyses).

Table 10-21. Analysis of All Stomach Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*6 (0.8)*	*1.14 (0.40,3.31)*	*0.804*
	Comparison	*1,172*	*8 (0.7)*		
Officer	Ranch Hand	302	1 (0.3)	0.30 (0.04,2.61)	0.277
	Comparison	461	5 (1.1)		
Enlisted Flyer	Ranch Hand	131	3 (2.3)	4.31 (0.44,41.93)	0.208
	Comparison	185	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	336	2 (0.6)	1.57 (0.22,11.19)	0.653
	Comparison	526	2 (0.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*0.73 (0.22,2.43)*	*0.609*
Officer	762	0.22 (0.02,1.99)	0.176
Enlisted Flyer	313	2.58 (0.24,27.52)	0.433
Enlisted Groundcrew	855	1.02 (0.13,7.98)	0.983

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	1 (0.7)	1.37 (0.63,2.98)	0.442
Medium	142	1 (0.7)		
High	140	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 10-21. Analysis of All Stomach Neoplasms (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
415	1.70 (0.69,4.24)	0.245

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for military occupation and cumulative ionizing radiation because of the sparse number of Ranch Hands with a neoplasm of the stomach. Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	8 (0.7)		
Background RH	350	3 (0.9)	1.27 (0.33,4.86)	0.727
Low RH	206	2 (1.0)	1.42 (0.30,6.75)	0.658
High RH	212	1 (0.5)	0.68 (0.08,5.52)	0.721
Low plus High RH	418	3 (0.7)	0.98 (0.24,3.97)	0.978

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	0.80 (0.18,3.48)	0.767
Low RH	205	0.81 (0.15,4.29)	0.802
High RH	210	0.49 (0.05,4.61)	0.533
Low plus High RH	415	0.63 (0.13,2.93)	0.553

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-21. Analysis of All Stomach Neoplasms (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
Low	259	2 (0.8)	1.14 (0.70,1.85)	0.600
Medium	253	2 (0.8)		
High	256	2 (0.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
763	1.04 (0.56,1.91)	0.910

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.20 *Malignant Systemic Neoplasms (Colon and Rectum)*

In the unadjusted analyses of Model 1, Ranch Hand officers had a significantly higher occurrence of a malignant systemic neoplasm of the colon or rectum versus Comparison officers (Table 10-22(a): Unadjusted RR=4.15, p=0.037). The prevalences were 2.6 percent and 0.7 percent for Ranch Hands and Comparisons, respectively. After covariate adjustment, the results remained significant (Table 10-22(b): Adjusted RR=4.66, p=0.044). All other Model 1 results were nonsignificant (Table 10-22(a,b): p>0.15 for all analyses).

The Model 3 unadjusted analyses of malignant systemic neoplasms of the colon and rectum displayed a significant difference between Ranch Hands in the low dioxin category and Comparisons. The occurrence of a malignant systemic neoplasm of the colon or rectum was higher for Ranch Hands in the low dioxin category (3.4%) than for Comparisons (0.9%) (Table 10-22(e): Unadjusted RR=3.74, p=0.009). The result was also significant after adjusting for covariates (Table 10-22(f): Adjusted RR=3.74, p=0.035). All other Model 3 contrasts were nonsignificant (Table 10-22(e,f): p≥0.24).

All results from the unadjusted and adjusted analyses of malignant systemic neoplasms of the colon and rectum for Models 2 and 4 were nonsignificant (Table 10-22(c,d,g,h): p>0.08 for all analyses).

Table 10-22. Analysis of Malignant Systemic Neoplasms (Colon and Rectum)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*12 (1.6)*	*1.84 (0.79,4.28)*	*0.155*
	Comparison	*1,172*	*10 (0.9)*		
Officer	Ranch Hand	302	8 (2.6)	4.15 (1.09,15.79)	0.037*
	Comparison	461	3 (0.7)		
Enlisted Flyer	Ranch Hand	131	1 (0.8)	0.47 (0.05,4.54)	0.511
	Comparison	185	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	336	3 (0.9)	1.18 (0.26,5.29)	0.833
	Comparison	526	4 (0.8)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*2.03 (0.68,6.00)*	*0.188*
Officer	762	4.66 (1.04,20.80)	0.044*
Enlisted Flyer	313	0.53 (0.05,5.77)	0.600
Enlisted Groundcrew	855	1.20 (0.23,6.38)	0.828

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	3 (2.2)	0.76 (0.44,1.32)	0.311
Medium	142	4 (2.8)		
High	140	2 (1.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
415	1.03 (0.52,2.05)	0.924

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the colon or rectum. Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	10 (0.9)		
Background RH	350	3 (0.9)	1.20 (0.33,4.42)	0.784
Low RH	206	7 (3.4)	3.74 (1.39,10.07)	0.009**
High RH	212	2 (0.9)	0.93 (0.20,4.34)	0.927
Low plus High RH	418	9 (2.2)	1.85 (0.66,5.14)	0.240

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	1.14 (0.26,5.06)	0.863
Low RH	205	3.74 (1.10,12.73)	0.035*
High RH	210	1.21 (0.21,7.02)	0.831
Low plus High RH	415	2.11 (0.60,7.40)	0.242

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-22. Analysis of Malignant Systemic Neoplasms (Colon and Rectum) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Yes**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	259	2 (0.8)	1.11 (0.78,1.57)	0.559
Medium	253	6 (2.4)		
High	256	4 (1.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
763	1.60 (0.92,2.78)	0.087

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.21 *Malignant Systemic Neoplasms (Urinary System)*

In the unadjusted analyses of Model 1 of occurrence of malignant systemic neoplasms of the urinary system, the difference between Ranch Hands and Comparisons across all occupations was significant (Table 10-23(a): Unadjusted RR=2.32, p=0.023). More malignant systemic neoplasms of the urinary system occurred in Ranch Hands than in Comparisons (2.3% versus 1.0%, respectively). After adjusting for covariates, the result remained significant (Table 10-23(b): Adjusted RR=3.02, p=0.018). Also, the adjusted analysis of Model 1 revealed a significant difference between Ranch Hand and Comparison officers (Table 10-23(b): Adjusted RR=3.59, p=0.049). Again, more malignant systemic neoplasms of the urinary system occurred among Ranch Hands than among Comparisons (2.6% versus 1.1%, respectively). All other Model 1 contrasts were nonsignificant (Table 10-23(a,b): p≥0.09 for all analyses).

The unadjusted analysis of Model 2 did not reveal significant findings (Table 10-23(c): p=0.983). After covariate adjustment, the results were significant, where the prevalence of malignant systemic neoplasms of the urinary system among Ranch Hands increased as initial dioxin increased (Table 10-23(d): Adjusted RR=2.08, p=0.049). The percentages of Ranch Hands with a malignant systemic neoplasm of the urinary system were 1.5, 2.8, and 2.1 among those in the low, medium, and high initial dioxin categories, respectively.

A significantly greater percentage of Ranch Hands in the background and low dioxin categories had a malignant systemic neoplasm of the urinary system, relative to Comparisons, in the unadjusted Model 3 analyses (Table 10-23(e): Unadjusted RR=2.77, p=0.023 for the background dioxin category; Unadjusted RR=2.80, p=0.042 for the low dioxin category). The percentages of participants with a malignant

systemic neoplasm of the urinary system were 1.0 for Comparisons and 2.6 and 2.9 for Ranch Hands in the background and low dioxin categories, respectively. In the adjusted analyses, the only significant result occurred among the Ranch Hands in the background dioxin category (Table 10-23(f): Adjusted RR=3.62, p=0.018). All other Model 3 contrasts were nonsignificant (Table 10-23(e,f): p>0.10 for all analyses).

There were no significant results in the unadjusted and adjusted Model 4 analyses (Table 10-23(g,h): p>0.43 for both analyses).

Table 10-23. Analysis of Malignant Systemic Neoplasms (Urinary System)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*18 (2.3)*	*2.32 (1.11,4.84)*	*0.023**
	Comparison	*1,172*	*12 (1.0)*		
Officer	Ranch Hand	302	8 (2.6)	2.48 (0.80,7.66)	0.114
	Comparison	461	5 (1.1)		
Enlisted Flyer	Ranch Hand	131	4 (3.1)	5.80 (0.64,52.46)	0.118
	Comparison	185	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	336	6 (1.8)	1.58 (0.50,4.93)	0.434
	Comparison	526	6 (1.1)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*3.02 (1.16,7.89)*	*0.018**
Officer	762	3.59 (1.01,12.81)	0.049*
Enlisted Flyer	313	7.36 (0.73,73.97)	0.090
Enlisted Groundcrew	855	1.77 (0.45,6.91)	0.413

*: Statistically significant (0.010<p-value≤0.050).

Note: Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the urinary system.

Table 10-23. Analysis of Malignant Systemic Neoplasms (Urinary System) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Yes**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	136	2 (1.5)	1.01 (0.62,1.63)	0.983
Medium	142	4 (2.8)		
High	140	3 (2.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
415	2.08 (0.99,4.37)	0.049*

[a]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the urinary system. Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	12 (1.0)		
Background RH	350	9 (2.6)	2.77 (1.15,6.68)	0.023*
Low RH	206	6 (2.9)	2.80 (1.04,7.58)	0.042*
High RH	212	3 (1.4)	1.29 (0.36,4.64)	0.694
Low plus High RH	418	9 (2.2)	1.89 (0.76,4.70)	0.169

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	3.62 (1.24,10.51)	0.018*
Low RH	205	2.83 (0.81,9.88)	0.102
High RH	210	2.20 (0.50,9.69)	0.296
Low plus High RH	415	2.49 (0.79,7.83)	0.117

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.010 < $ p-value ≤ 0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt $<$ initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the urinary system.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	7 (2.7)	0.89 (0.66,1.20)	0.438
Medium	253	6 (2.4)		
High	256	5 (2.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤ 7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	0.87 (0.60,1.26)	0.459

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the urinary system. Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.22 Malignant Systemic Neoplasms (Kidney and Ureter)

In both the unadjusted and adjusted analyses of malignant systemic neoplasms of the kidney or ureter for Models 1 through 3, there were no significant findings (Table 10-24(a-f): p>0.06 for all analyses). There were also no significant findings in the unadjusted analysis of Model 4 (Table 10-24(g): p=0.138). After covariate adjustment, the results for Model 4 became significant, where the prevalence of malignant systemic neoplasms of the kidney or ureter decreased as 1987 dioxin increased (Table 10-24(h): Adjusted RR=0.55, p=0.048). The percentages of Ranch Hands with a malignant systemic neoplasm of the kidney or ureter for the low, medium, and high 1987 dioxin levels were 1.2, 0.4, and 1.2, respectively.

Table 10-24. Analysis of Malignant Systemic Neoplasms (Kidney and Ureter)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*7 (0.9)*	*2.68 (0.78,9.19)*	*0.107*
	Comparison	*1,172*	*4 (0.3)*		
Officer	Ranch Hand	302	2 (0.7)	3.07 (0.28,33.97)	0.361
	Comparison	461	1 (0.2)		
Enlisted Flyer	Ranch Hand	131	1 (0.8)	--	0.862[a]
	Comparison	185	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	336	4 (1.2)	2.10 (0.47,9.44)	0.333
	Comparison	526	3 (0.6)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the kidney or ureter.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the kidney or ureter.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*2.87 (0.57,14.50)*	*0.181*
Officer	762	4.21 (0.31,56.80)	0.279
Enlisted Flyer	313	--	--
Enlisted Groundcrew	855	1.87 (0.27,12.70)	0.523

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the kidney or ureter.

Note: Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the kidney or ureter.

Table 10-24. Analysis of Malignant Systemic Neoplasms (Kidney and Ureter) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	0 (0.0)	1.05 (0.47,2.33)	0.903
Medium	142	2 (1.4)		
High	140	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
415	1.89 (0.38,9.43)	0.426

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the kidney or ureter. Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	4 (0.3)		
Background RH	350	4 (1.1)	3.70 (0.91,15.08)	0.068
Low RH	206	2 (1.0)	2.75 (0.50,15.16)	0.247
High RH	212	1 (0.5)	1.28 (0.14,11.56)	0.829
Low plus High RH	418	3 (0.7)	1.86 (0.39,8.91)	0.437

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	5.17 (0.88,30.37)	0.069
Low RH	205	2.03 (0.17,24.09)	0.574
High RH	210	1.33 (0.11,16.17)	0.822
Low plus High RH	415	1.64 (0.22,12.31)	0.630

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of the kidney or ureter.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	3 (1.2)	0.69 (0.43,1.13)	0.138
Medium	253	1 (0.4)		
High	256	3 (1.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	0.55 (0.31,0.98)	0.048*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value$\leq$0.050).

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the kidney or ureter. Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.23   Malignant Systemic Neoplasms (Prostate)

All results from the Model 1 and Model 4 analyses, both unadjusted and adjusted, of malignant systemic neoplasms of the prostate were nonsignificant (Table 10-25(a,b,g,h): p>0.08 for all analyses).

A significant inverse association between initial dioxin and the occurrence of malignant systemic neoplasms of the prostate was found in the unadjusted Model 2 analysis (Table 10-25(c): Unadjusted RR=0.54, p<0.001). After adjusting for covariates, the association was nonsignificant (Table 10-25(d): p=0.069).

The Model 3 unadjusted analysis revealed a significant difference in the occurrence of a malignant systemic neoplasm of the prostate between Ranch Hands in the low dioxin category and Comparisons (Table 10-25(e): Unadjusted RR=2.00, p=0.007). More Ranch Hands than Comparisons had a malignant systemic neoplasm of the prostate (10.7% versus 5.7%, respectively). After covariate adjustment, this result remained significant (Table 10-25(f): Adjusted RR=1.85, p=0.048). All other Model 3 contrasts, both unadjusted and adjusted, were nonsignificant (Table 10-25(e,f): p>0.20 for all analyses).

Table 10-25. Analysis of Malignant Systemic Neoplasms (Prostate)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes		Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*53*	*(6.9)*	*1.22 (0.84,1.77)*	*0.296*
	Comparison	*1,172*	*67*	*(5.7)*		
Officer	Ranch Hand	302	26	(8.6)	1.31 (0.76,2.25)	0.334
	Comparison	461	31	(6.7)		
Enlisted Flyer	Ranch Hand	131	14	(10.7)	2.09 (0.90,4.87)	0.086
	Comparison	185	10	(5.4)		
Enlisted Groundcrew	Ranch Hand	336	13	(3.9)	0.77 (0.39,1.53)	0.460
	Comparison	526	26	(4.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*1.28 (0.80,2.05)*	*0.303*
Officer	762	1.42 (0.77,2.62)	0.257
Enlisted Flyer	313	2.13 (0.85,5.35)	0.106
Enlisted Groundcrew	855	0.77 (0.36,1.67)	0.512

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a,b]**	**p-Value**
Low	136	16 (11.8)	0.54 (0.37,0.79)	<0.001**
Medium	142	12 (8.5)		
High	140	3 (2.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
415	0.67 (0.43,1.05)	0.069

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	67 (5.7)		
Background RH	350	22 (6.3)	1.06 (0.64,1.74)	0.834
Low RH	206	22 (10.7)	2.00 (1.21,3.32)	0.007**
High RH	212	9 (4.2)	0.76 (0.37,1.55)	0.454
Low plus High RH	418	31 (7.4)	1.23 (0.76,1.97)	0.399

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	1.03 (0.58,1.83)	0.928
Low RH	205	1.85 (1.00,3.39)	0.048*
High RH	210	1.16 (0.51,2.62)	0.721
Low plus High RH	415	1.46 (0.82,2.61)	0.202

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.010 < $p-value$\leq 0.050$).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	17 (6.6)	0.88 (0.74,1.05)	0.157
Medium	253	24 (9.5)		
High	256	12 (4.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	0.92 (0.72,1.18)	0.517

[a]Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.24 *Malignant Systemic Neoplasms (Penis and Other Male Genital Organs)*

There were no significant findings among the Model 1 unadjusted analyses and Model 2 unadjusted and adjusted analyses of malignant systemic neoplasms of the penis and other male genital organs (Table 10-26(a,c,d): p>0.05 for all analyses). Adjusted analyses of Models 1 and 3 could not be performed because of the limited number of neoplasms. In the unadjusted analysis of Model 3, a significant difference in the occurrence of a malignant systemic neoplasm of the penis or other male genital organs was found between Ranch Hands in the high dioxin category and Comparisons (Table 10-26(e):

p=0.019). No Comparisons had malignant systemic neoplasms of the penis and other male genital organs compared to 0.9 percent of Ranch Hands in the high dioxin category.

The Model 4 unadjusted analysis did not reveal significant results (Table 10-26(g): p=0.053). After covariate adjustment, a significant positive relation was found between 1987 dioxin and the occurrence of malignant systemic neoplasms of the penis and other male genital organs (Table 10-26(h): Adjusted RR=3.52, p=0.017). Two Ranch Hands in the high 1987 dioxin category had a malignant systemic neoplasm of the penis or other male genital organs, whereas no Ranch Hands in the low 1987 dioxin category or medium 1987 dioxin category had a neoplasm of this type.

Table 10-26. Analysis of Malignant Systemic Neoplasms (Penis and Other Male Genital Organs)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*2 (0.3)*	*--*	*0.306[a]*
	Comparison	*1,939*	*0 (0.0)*		
Officer	Ranch Hand	302	0 (0.0)	--	--
	Comparison	461	0 (0.0)		
Enlisted Flyer	Ranch Hand	131	2 (1.5)	--	0.334[a]
	Comparison	185	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	336	0 (0.0)	--	--
	Comparison	526	0 (0.0)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the penis or other male genital organs.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the penis or other male genital organs.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*--*	*--*
Officer	762	--	--
Enlisted Flyer	313	--	--
Enlisted Groundcrew	855	--	--

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the penis or other male genital organs.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	0 (0.0)	2.15 (0.87,5.33)	0.103
Medium	142	0 (0.0)		
High	140	2 (1.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
415	2.93 (0.82,10.42)	0.058

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, cumulative ionizing radiation exposure, and cumulative herbicide exposure because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the penis or other male genital organs.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
Comparison	1,172	0 (0.0)		
Background RH	350	0 (0.0)	--	--
Low RH	206	0 (0.0)	--	--
High RH	212	2 (0.9)	--	0.019*[a]
Low plus High RH	418	2 (0.5)	--	0.117[a]

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasms of the penis or other male genital organs.

*: Statistically significant (0.010<p-value≤0.050).

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the penis or other male genital organs.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
Comparison	1,166		
Background RH	348	--	--
Low RH	205	--	--
High RH	210	--	--
Low plus High RH	415	--	--

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the penis or other male genital organs.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	0 (0.0)	2.22 (0.97,5.09)	0.053
Medium	253	0 (0.0)		
High	256	2 (0.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin) Adjusted Relative Risk	
n	(95% C.I.)[a]	p-Value
763	3.52 (1.04,11.91)	0.017*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value$\leq$0.050).

Note: Results were not adjusted for race, military occupation, cumulative ionizing radiation exposure, and cumulative herbicide exposure because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the penis or other male genital organs.

10.2.2.1.25   Malignant Systemic Neoplasms (Testicles)

All unadjusted and adjusted analyses performed for malignant systemic neoplasms of the testicles using Models 1, 2, and 4 were nonsignificant (Table 10-27(a-d,g,h): p>0.12 for all analyses). Due to a sparse number of neoplasms, the adjusted analyses of Model 1 could not be performed.

Significant differences were found in the unadjusted Model 3 analysis between Ranch Hands in the low dioxin category and Comparisons, and between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 10-27(e): p=0.017 and p=0.025, respectively). The prevalences were 1.0 percent for Ranch Hands in the low dioxin category and 0.7 percent for Ranch Hands in the low and high dioxin categories combined. There were no occurrences of malignant systemic neoplasms of the testicles among Comparisons. The adjusted Model 3 analyses were not possible because of the sparse number of neoplasms of the testicles.

Table 10-27. Analysis of Malignant Systemic Neoplasms (Testicles)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*3 (0.4)*	*--*	*0.121*[a]
	Comparison	*1,938*	*0 (0.0)*		
Officer	Ranch Hand	302	1 (0.3)	--	0.831[a]
	Comparison	461	0 (0.0)		
Enlisted Flyer	Ranch Hand	131	1 (0.8)	--	0.862[a]
	Comparison	185	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	336	1 (0.3)	--	0.821[a]
	Comparison	526	0 (0.0)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the testicles.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the testicles.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*--*	*--*
Officer	762	--	--
Enlisted Flyer	313	--	--
Enlisted Groundcrew	855	--	--

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the testicles.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	1 (0.7)	0.65 (0.22,1.92)	0.399
Medium	142	2 (1.4)		
High	140	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
415	0.75 (0.23,2.44)	0.615

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and cumulative herbicide exposure because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the testicles.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
Comparison	1,172	0 (0.0)		
Background RH	350	0 (0.0)	--	--
Low RH	206	2 (1.0)	--	0.017*[a]
High RH	212	1 (0.5)	--	0.335[a]
Low plus High RH	418	3 (0.7)	--	0.025*[a]

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the testicles.

*: Statistically significant (0.010<p-value≤0.050).

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the testicles.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
Comparison	1,166		
Background RH	348	--	--
Low RH	205	--	--
High RH	210	--	--
Low plus High RH	415	--	--

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the testicles.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	0 (0.0)	1.23 (0.63,2.41)	0.551
Medium	253	1 (0.4)		
High	256	2 (0.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	1.39 (0.56,3.45)	0.470

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race and cumulative herbicide exposure because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the testicles.

10.2.2.1.26   *Malignant Systemic Neoplasms (Bone and Articular Cartilage)*

There were no significant results for the unadjusted analyses of malignant systemic neoplasms of the bone and articular cartilage for Models 1 and 3 (Table 10-28(a,e): p>0.26 for all analyses). No unadjusted analyses could be performed for Model 2 or Model 4, and no adjusted analyses could be performed for Models 1 through 4.

Table 10-28. Analysis of Malignant Systemic Neoplasms (Bone and Articular Cartilage)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*0 (0.0)*	*--*	*0.267*[a]
	Comparison	*1,172*	*4 (0.3)*		
Officer	Ranch Hand	302	0 (0.0)	--	0.999[a]
	Comparison	461	1 (0.2)		
Enlisted Flyer	Ranch Hand	131	0 (0.0)	--	0.636[a]
	Comparison	185	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	336	0 (0.0)	--	0.999[a]
	Comparison	526	1 (0.2)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the bone or articular cartilage.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the bone or articular cartilage.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*--*	*--*
Officer	762	--	--
Enlisted Flyer	313	--	--
Enlisted Groundcrew	855	--	--

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the bone or articular cartilage.

**Table 10-28. *Analysis of Malignant Systemic Neoplasms (Bone and Articular Cartilage)*
*(Continued)***

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
Low	136	0 (0.0)	--	--
Medium	142	0 (0.0)		
High	140	0 (0.0)		

--: Results were not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the bone or articular cartilage.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
415	--	--

--: Results were not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the bone or articular cartilage.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
Comparison	1,172	4 (0.3)		
Background RH	350	0 (0.0)	--	0.617[a]
Low RH	206	0 (0.0)	--	0.891[a]
High RH	212	0 (0.0)	--	0.876[a]
Low plus High RH	418	0 (0.0)	--	0.531[a]

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of the bone or articular cartilage.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the bone or articular cartilage.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
Comparison	1,166		
Background RH	348	--	--
Low RH	205	--	--
High RH	210	--	--
Low plus High RH	415	--	--

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of the bone or articular cartilage.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
Low	259	0 (0.0)	--	--
Medium	253	0 (0.0)		
High	256	0 (0.0)		

--: Results were not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the bone or articular cartilage.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	(95% C.I.)	p-Value
763	--	--

--: Results were not presented because of the sparse number of Ranch Hands with a malignant systemic neoplasm of the bone or articular cartilage.

10.2.2.1.27   Malignant Systemic Neoplasms (Connective and Other Soft Tissues)

All results from the unadjusted and adjusted Model 1 through 4 analyses performed for malignant systemic neoplasms of connective and other soft tissues were nonsignificant (Table 10-29(a-h): p>0.10 for each analysis).

Table 10-29. Analysis of Malignant Systemic Neoplasms (Connective and Other Soft Tissues)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*1 (0.1)*	*0.25 (0.03,2.11)*	*0.141*
	Comparison	*1,172*	*6 (0.5)*		
Officer	Ranch Hand	302	0 (0.0)	--	0.416[a]
	Comparison	461	3 (0.7)		
Enlisted Flyer	Ranch Hand	131	1 (0.8)	1.42 (0.09,22.84)	0.807
	Comparison	185	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	336	0 (0.0)	--	0.685[a]
	Comparison	526	2 (0.4)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of connective or other soft tissues.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of connective or other soft tissues.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*0.20 (0.02,1.84)*	*0.109*
Officer	762	--	--
Enlisted Flyer	313	1.28 (0.07,23.07)	0.866
Enlisted Groundcrew	855	--	--

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of connective or other soft tissues.

Note: Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of connective or other soft tissues.

Table 10-29. Analysis of Malignant Systemic Neoplasms (Connective and Other Soft Tissues) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	0 (0.0)	2.50 (0.70,8.93)	0.159
Medium	142	0 (0.0)		
High	140	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	2.62 (0.67,10.23)	0.155

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for age, military occupation, race, cumulative ionizing radiation exposure, cumulative herbicide exposure, and lifetime alcohol history because of the sparse number of Ranch Hands with a malignant systemic neoplasm of connective or other soft tissues.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	6 (0.5)		
Background RH	350	0 (0.0)	--	0.392[c]
Low RH	206	0 (0.0)	--	0.649[c]
High RH	212	1 (0.5)	0.82 (0.10,6.98)	0.858
Low plus High RH	418	1 (0.2)	--	0.770[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a malignant systemic neoplasm of connective or other soft tissues.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of connective or other soft tissues.

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	--	--
Low RH	205	--	--
High RH	210	0.95 (0.09,10.22)	0.966
Low plus High RH	415	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with a malignant systemic neoplasm of connective or other soft tissues.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of connective or other soft tissues.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	0 (0.0)	2.35 (0.72,7.62)	0.144
Medium	253	0 (0.0)		
High	256	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
767	2.33 (0.74,7.37)	0.146

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for age, military occupation, race, cumulative ionizing radiation exposure, cumulative herbicide exposure, and lifetime alcohol history because of the sparse number of Ranch Hands with a malignant systemic neoplasm of connective or other soft tissues.

10.2.2.1.28   Carcinoma in Situ (Breast, Digestive Organs, Respiratory, Prostate, Penis and Other Male Genitals, and Bladder and Other and Nonspecified Urinary)

All results from the unadjusted and adjusted analyses performed of Models 1, 2, and 4 of carcinoma in situ (breast, digestive organs, respiratory, prostate, penis and other male genitals, and bladder and other and nonspecified urinary) were nonsignificant (Table 10-30(a-d,g,h): p>0.06 for all analyses). The unadjusted Model 3 analyses were nonsignificant, but after adjustment for covariates, a significant result was found for the Model 3 analysis of carcinoma in situ between Ranch Hands in the low dioxin category and Comparisons (Table 10-30(f): Adjusted RR=20.75, p=0.027). Three Ranch Hands in the low dioxin category (1.5%) and six Comparisons (0.5%) had a carcinoma in situ.

Table 10-30. Analysis of Carcinoma in Situ (Breast, Digestive Organs, Respiratory, Prostate, Penis and Other Male Genitals, and Bladder and Other and Nonspecified Urinary)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*4 (0.5)*	*1.02 (0.29,3.61)*	*0.980*
	Comparison	*1,172*	*6 (0.5)*		
Officer	Ranch Hand	302	2 (0.7)	3.07 (0.28,33.97)	0.361
	Comparison	461	1 (0.2)		
Enlisted Flyer	Ranch Hand	131	2 (1.5)	0.94 (0.15,5.71)	0.947
	Comparison	185	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	336	0 (0.0)	--	0.685[a]
	Comparison	526	2 (0.4)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a carcinoma in situ.

--: Results were not presented because of the sparse number of participants with a carcinoma in situ.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*4.71 (0.56,39.47)*	*0.137*
Officer	762	17.42 (0.82,372.10)	0.067
Enlisted Flyer	313	6.86 (0.35,134.80)	0.205
Enlisted Groundcrew	855	--	--

--: Results were not presented because of the sparse number of participants with a carcinoma in situ.

Note: Results were not adjusted for race because of the sparse number of participants with a carcinoma in situ.

Table 10-30. Analysis of Carcinoma in Situ (Breast, Digestive Organs, Respiratory,
Prostate, Penis and Other Male Genitals, and Bladder and Other and
Nonspecified Urinary) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	2 (1.5)	0.45 (0.12,1.65)	0.157
Medium	142	1 (0.7)		
High	140	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
415	0.41 (0.09,1.91)	0.177

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for military occupation, race, and cumulative herbicide exposure because of the
sparse number of Ranch Hands with a carcinoma in situ.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	6 (0.5)		
Background RH	350	1 (0.3)	0.56 (0.07,4.71)	0.594
Low RH	206	3 (1.5)	2.87 (0.71,11.57)	0.139
High RH	212	0 (0.0)	--	0.634[c]
Low plus High RH	418	3 (0.7)	--	0.919[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of
 participants with a carcinoma in situ.

--: Results were not presented because of the sparse number of participants with a carcinoma in situ.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	3.23 (0.20,51.07)	0.405
Low RH	205	20.75 (1.40,307.55)	0.027*
High RH	210	--	--
Low plus High RH	415	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with a carcinoma in situ.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race because of the sparse number of participants with a carcinoma in situ.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	1 (0.4)	1.03 (0.56,1.88)	0.933
Medium	253	3 (1.2)		
High	256	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	1.18 (0.59,2.37)	0.646

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for military occupation, race, and cumulative herbicide exposure because of the sparse number of Ranch Hands with a carcinoma in situ.

10.2.2.1.29 Hodgkin's Disease

All unadjusted and adjusted analyses of Hodgkin's disease performed for Models 1, 3, and 4 were nonsignificant (Table 10-31(a-h): p>0.42 for all analyses). Unadjusted and adjusted analyses for Model 2 were unable to be performed because no Ranch Hands with an initial dioxin estimate had a history of Hodgkin's disease.

Table 10-31. Analysis of Hodgkin's Disease

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*1 (0.1)*	*1.52 (0.10,24.41)*	*0.766*
	Comparison	*1,172*	*1 (0.1)*		
Officer	Ranch Hand	302	1 (0.3)	--	0.831[a]
	Comparison	461	0 (0.0)		
Enlisted Flyer	Ranch Hand	131	0 (0.0)	--	--
	Comparison	185	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	336	0 (0.0)	--	0.999[a]
	Comparison	526	1 (0.2)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with Hodgkin's disease.

--: Results were not presented because of the sparse number of participants with Hodgkin's disease.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*1.47 (0.09,24.30)*	*0.786*
Officer	762	--	--
Enlisted Flyer	313	--	--
Enlisted Groundcrew	855	--	--

--: Results were not presented because of the sparse number of participants with Hodgkin's disease.

Note: Results were not adjusted for race, military occupation, cumulative ionizing radiation exposure, and cumulative herbicide exposure because of the sparse number of participants with Hodgkin's disease.

Table 10-31. Analysis of Hodgkin's Disease (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
Low	136	0 (0.0)	--	--
Medium	142	0 (0.0)		
High	140	0 (0.0)		

--: Results were not presented because of the sparse number of Ranch Hands with Hodgkin's disease.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
415	--	--

--: Results were not presented because of the sparse number of Ranch Hands with Hodgkin's disease.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	1 (0.1)		
Background RH	350	1 (0.3)	3.14 (0.19,52.10)	0.424
Low RH	206	0 (0.0)	--	0.999[c]
High RH	212	0 (0.0)	--	0.999[c]
Low plus High RH	418	0 (0.0)	--	0.999[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with Hodgkin's disease.

--: Results were not presented because of the sparse number of participants with Hodgkin's disease.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-31. Analysis of Hodgkin's Disease (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	3.10 (0.18,53.55)	0.437
Low RH	205	--	--
High RH	210	--	--
Low plus High RH	415	--	--

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race, military occupation, cumulative ionizing radiation exposure, and cumulative herbicide exposure because of the sparse number of participants with Hodgkin's disease.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	1 (0.4)	0.73 (0.20,2.62)	0.628
Medium	253	0 (0.0)		
High	256	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for $\log_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	0.50 (0.01,16.93)	0.653

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, military occupation, cumulative ionizing radiation exposure, cumulative herbicide exposure, and lifetime cigarette smoking history because of the sparse number of Ranch Hands with Hodgkin's disease.

10.2.2.1.30 Leukemia

There were no significant findings for the analyses of leukemia performed for Models 1 and 3, both unadjusted and adjusted (Table 10-32(a,b,e,f): p>0.27 for all analyses). Model 2 analyses were not performed because of the sparse number of Ranch Hands with leukemia.

For the unadjusted analysis of Model 4, a significant inverse relation was found between 1987 dioxin and occurrence of leukemia (Table 10-32(g): Unadjusted RR=0.43, p=0.008). The percentages of Ranch Hands with leukemia were 1.2 for those in the low 1987 dioxin category and 0.4 for those in the medium 1987 dioxin category. There were no occurrences of leukemia among those Ranch Hands in the high 1987 dioxin category. After covariate adjustment, the result remained significant (Table 10-32(h): Adjusted RR=0.40, p=0.004).

Table 10-32. Analysis of Leukemia

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*4 (0.5)*	*1.02 (0.29,3.61)*	*0.980*
	Comparison	*1,172*	*6 (0.5)*		
Officer	Ranch Hand	302	3 (1.0)	1.15 (0.25,5.16)	0.859
	Comparison	461	4 (0.9)		
Enlisted Flyer	Ranch Hand	131	1 (0.8)	--	0.862[a]
	Comparison	185	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	336	0 (0.0)	--	0.685[a]
	Comparison	526	2 (0.4)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with leukemia.

--: Results were not presented because of the sparse number of participants with leukemia.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*1.17 (0.23,5.93)*	*0.845*
Officer	762	1.31 (0.22,7.93)	0.770
Enlisted Flyer	313	--	--
Enlisted Groundcrew	855	--	--

--: Results were not presented because of the sparse number of participants with leukemia.

Note: Results were not adjusted for race because of the sparse number of participants with leukemia.

Table 10-32. Analysis of Leukemia (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
Low	136	0 (0.0)	--	--
Medium	142	0 (0.0)		
High	140	0 (0.0)		

--: Results were not presented because of the sparse number of Ranch Hands with leukemia.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
415	--	--

--: Results were not presented because of the sparse number of Ranch Hands with leukemia.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	6 (0.5)		
Background RH	350	4 (1.1)	2.06 (0.57,7.44)	0.271
Low RH	206	0 (0.0)	--	0.649[c]
High RH	212	0 (0.0)	--	0.634[c]
Low plus High RH	418	0 (0.0)	--	0.317[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with leukemia.

--: Results were not presented because of the sparse number of participants with leukemia.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-32. Analysis of Leukemia (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	2.06 (0.42,10.04)	0.371
Low RH	205	--	--
High RH	210	--	--
Low plus High RH	415	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with leukemia.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race because of the sparse number of participants with leukemia.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	3 (1.2)	0.43 (0.23,0.79)	0.008**
Medium	253	1 (0.4)		
High	256	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	0.40 (0.21,0.74)	0.004**

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Results were not adjusted for race, military occupation, and cumulative herbicide exposure because of the sparse number of Ranch Hands with leukemia.

10.2.2.1.31   Other Malignant Systemic Neoplasms (Lymphoid and Histiocytic Tissue)

All results from the unadjusted and adjusted analyses for malignant systemic neoplasms of lymphoid and histiocytic tissue using Models 1 through 4 were nonsignificant (Table 10-33(a-h): p>0.13 for all analyses).

Table 10-33. Analysis of Other Malignant Systemic Neoplasms (Lymphoid and Histiocytic Tissue)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*6 (0.8)*	*1.02 (0.36,2.87)*	*0.976*
	Comparison	*1,172*	*9 (0.8)*		
Officer	Ranch Hand	302	3 (1.0)	2.30 (0.38,13.86)	0.362
	Comparison	461	2 (0.4)		
Enlisted Flyer	Ranch Hand	131	1 (0.8)	0.35 (0.04,3.15)	0.348
	Comparison	185	4 (2.2)		
Enlisted Groundcrew	Ranch Hand	336	2 (0.6)	1.04 (0.17,6.28)	0.963
	Comparison	526	3 (0.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*0.74 (0.23,2.36)*	*0.606*
Officer	762	2.00 (0.31,12.97)	0.467
Enlisted Flyer	313	0.22 (0.02,2.21)	0.199
Enlisted Groundcrew	855	0.71 (0.11,4.63)	0.719

Note: Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of lymphoid and histiocytic tissue.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	3 (2.2)	0.67 (0.30,1.54)	0.312
Medium	142	1 (0.7)		
High	140	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
415	0.83 (0.33,2.13)	0.697

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic neoplasm of lymphoid and histiocytic tissue. Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	9 (0.8)		
Background RH	350	1 (0.3)	0.39 (0.05,3.12)	0.377
Low RH	206	4 (1.9)	2.50 (0.76,8.22)	0.131
High RH	212	1 (0.5)	0.58 (0.07,4.64)	0.610
Low plus High RH	418	5 (1.2)	1.19 (0.33,4.35)	0.788

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	0.31 (0.04,2.65)	0.283
Low RH	205	1.56 (0.42,5.85)	0.508
High RH	210	0.39 (0.04,3.55)	0.404
Low plus High RH	415	0.77 (0.19,3.22)	0.725

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

    Results were not adjusted for race because of the sparse number of participants with a malignant systemic neoplasm of lymphoid and histiocytic tissue.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	1 (0.4)	0.91 (0.55,1.52)	0.727
Medium	253	3 (1.2)		
High	256	2 (0.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	0.99 (0.53,1.86)	0.985

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with a malignant systemic
neoplasm of lymphoid and histiocytic tissue. Results were not adjusted for cumulative herbicide exposure
because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.2.2.1.32   Lymphoreticular Sarcoma

There were no significant findings in the analyses of Models 1, 3, and 4 of lymphoreticular sarcoma
(Table 10-34(a,b,e-h): p>0.53 for all analyses). Unadjusted and adjusted Model 2 analyses were not
performed because of the sparse number of Ranch Hands with lymphoreticular sarcoma.

Table 10-34. Analysis of Lymphoreticular Sarcoma

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*1 (0.1)*	*0.51 (0.05,4.89)*	*0.537*
	Comparison	*1,172*	*3 (0.3)*		
Officer	Ranch Hand	302	1 (0.3)	0.51 (0.05,4.90)	0.557
	Comparison	461	3 (0.7)		
Enlisted Flyer	Ranch Hand	131	0 (0.0)	--	--
	Comparison	185	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	336	0 (0.0)	--	--
	Comparison	526	0 (0.0)		

--: Results were not presented because of the sparse number of participants with lymphoreticular sarcoma.

Table 10-34. Analysis of Lymphoreticular Sarcoma (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*0.67 (0.05,9.60)*	*0.765*
Officer	762	0.77 (0.05,10.98)	0.847
Enlisted Flyer	313	--	--
Enlisted Groundcrew	855	--	--

--: Results were not presented because of the sparse number of participants with lymphoreticular sarcoma.

Note: Results were not adjusted for race, military occupation, and cumulative ionizing radiation exposure because of the sparse number of participants with a lymphoreticular sarcoma.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
Low	136	0 (0.0)	--	--
Medium	142	0 (0.0)		
High	140	0 (0.0)		

--: Results were not presented because of the sparse number of Ranch Hands with lymphoreticular sarcoma.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
415	--	--

--: Results were not presented because of the sparse number of Ranch Hands with lymphoreticular sarcoma.

Table 10-34. Analysis of Lymphoreticular Sarcoma (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	3 (0.3)		
Background RH	350	1 (0.3)	0.91 (0.09,8.96)	0.939
Low RH	206	0 (0.0)	--	0.999[c]
High RH	212	0 (0.0)	--	0.999[c]
Low plus High RH	418	0 (0.0)	--	0.705[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of
 participants with lymphoreticular sarcoma.

--: Results were not presented because of the sparse number of participants with lymphoreticular sarcoma.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	348	1.05 (0.08,13.63)	0.973
Low RH	205	--	--
High RH	210	--	--
Low plus High RH	415	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with lymphoreticular sarcoma.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

  Results were not adjusted for race, military occupation, and cumulative ionizing radiation exposure because
  of the sparse number of participants with a lymphoreticular sarcoma.

Table 10-34. Analysis of Lymphoreticular Sarcoma (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	0 (0.0)	0.83 (0.24,2.95)	0.776
Medium	253	1 (0.4)		
High	256	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	1.02 (0.20,5.22)	0.981

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, military occupation, cumulative ionizing radiation exposure, and cumulative herbicide exposure because of the sparse number of Ranch Hands with a lymphoreticular sarcoma.

10.2.2.1.33   Skin and Systemic Neoplasms

The Model 1 unadjusted analyses of skin and systemic neoplasms revealed a significant difference between Ranch Hands and Comparisons when examined across all occupations (Table 10-35(a): Unadjusted RR=1.22, p=0.042). After covariate adjustment, the result was no longer significant (Table 10-35(b): p=0.491). All other Model 1 analyses, both unadjusted and adjusted, were nonsignificant (Table 10-35(a,b): p>0.14 for all analyses).

A significant inverse association between initial dioxin and the occurrence of skin or systemic neoplasms was found in the Model 2 unadjusted analysis (Table 10-35(c): Unadjusted RR=0.82, p=0.011). After adjusting for covariates, the result was nonsignificant (Table 10-35(d): p=0.372).

In the Model 3 unadjusted analyses, a significantly higher percentage of Ranch Hands in the low dioxin category had an occurrence of a skin or a systemic neoplasm, relative to Comparisons (Table 10-35(e): Unadjusted RR=1.74; p=0.001). After adjusting for covariates, the result remained significant (Table 10-35(f): Adjusted RR=1.46, p=0.048). The percentages of Ranch Hands in the low dioxin category and Comparisons exhibiting a skin or a systemic neoplasm were 73.8 and 61.7, respectively. All other Model 3 contrasts, as well as the results from the Model 4 analyses, were nonsignificant (Table 10-35(e-h): p≥0.08 for all analyses).

Table 10-35. Analysis of Skin and Systemic Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*759*	*503 (66.3)*	*1.22 (1.01,1.48)*	*0.042**
	Comparison	*1,157*	*714 (61.7)*		
Officer	Ranch Hand	298	213 (71.5)	1.27 (0.92,1.75)	0.142
	Comparison	452	300 (66.4)		
Enlisted Flyer	Ranch Hand	128	91 (71.1)	1.29 (0.79,2.11)	0.306
	Comparison	183	120 (65.6)		
Enlisted Groundcrew	Ranch Hand	333	199 (59.8)	1.15 (0.87,1.52)	0.321
	Comparison	522	294 (56.3)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*1.09 (0.86,1.38)*	*0.491*
Officer	746	1.12 (0.79,1.59)	0.517
Enlisted Flyer	309	1.10 (0.65,1.85)	0.725
Enlisted Groundcrew	847	1.06 (0.77,1.46)	0.734

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	133	102 (76.7)	0.82 (0.70,0.96)	0.011*
Medium	140	91 (65.0)		
High	138	80 (58.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 10-35. Analysis of Skin and Systemic Neoplasms (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk	
n	(95% C.I.)[a]	p-Value
409	0.91 (0.75,1.11)	0.372

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for the composite skin-reaction index.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,157	714 (61.7)		
Background RH	347	229 (66.0)	1.22 (0.95,1.57)	0.123
Low RH	202	149 (73.8)	1.74 (1.24,2.43)	0.001**
High RH	209	124 (59.3)	0.89 (0.66,1.21)	0.467
Low plus High RH	411	273 (66.4)	1.24 (0.97,1.58)	0.080

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,148		
Background RH	344	1.02 (0.76,1.37)	0.913
Low RH	201	1.46 (1.00,2.12)	0.048*
High RH	208	0.94 (0.66,1.34)	0.727
Low plus High RH	409	1.17 (0.87,1.56)	0.299

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-35. Analysis of Skin and Systemic Neoplasms (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	168 (65.4)	0.96 (0.87,1.05)	0.385
Medium	249	182 (73.1)		
High	252	152 (60.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
	Adjusted Relative Risk	
n	(95% C.I.)[a]	p-Value
753	1.03 (0.92,1.16)	0.594

[a]Relative risk for a twofold increase in 1987 dioxin.

10.2.2.1.34 Malignant Skin and Systemic Neoplasms

A significant difference between Ranch Hands and Comparisons was found in the unadjusted Model 1 analyses of malignant skin and systemic neoplasms for all occupations combined and for officers (Table 10-36(a): Unadjusted RR=1.22, p=0.049 overall; Unadjusted RR=1.41, p=0.027 for officers). All other Model 1 unadjusted analyses were nonsignificant (Table 10-36(a): p>0.05). After adjusting for covariates, all results were nonsignificant (Table 10-36(b): p>0.15 for all analyses).

The unadjusted analysis of Model 2 revealed a significant inverse relation between initial dioxin and occurrence of malignant skin or systemic neoplasms (Table 10-36(c): Unadjusted RR=0.76, p<0.001). After adjusting for covariates, the association was nonsignificant (Table 10-36(d): p=0.540).

Both the unadjusted and adjusted Model 3 analyses revealed a significant difference in the occurrence of malignant skin or systemic neoplasms between Ranch Hands in the low dioxin category and Comparisons (Table 10-36(e,f): Unadjusted RR=1.86, p<0.001; Adjusted RR=1.64, p=0.008, respectively). More Ranch Hands in the low dioxin category than Comparisons had malignant skin or systemic neoplasms (41.4% versus 27.4%, respectively). All other Model 3 contrasts and all unadjusted and adjusted results from the Model 4 analyses were nonsignificant (Table 10-36(e-h): p>0.08 for all analyses).

Table 10-36. Analysis of Malignant Skin and Systemic Neoplasms

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*762*	*241 (31.6)*	*1.22 (1.00,1.49)*	*0.049**
	Comparison	*1,159*	*318 (27.4*		
Officer	Ranch Hand	298	120 (40.3)	1.41 (1.04,1.91)	0.027*
	Comparison	454	147 (32.4)		
Enlisted Flyer	Ranch Hand	130	51 (39.2)	1.58 (0.98,2.55)	0.058
	Comparison	183	53 (29.0)		
Enlisted Groundcrew	Ranch Hand	334	70 (21.0)	0.91 (0.65,1.27)	0.570
	Comparison	522	118 (22.6)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,906*	*1.14 (0.88,1.47)*	*0.329*
Officer	748	1.28 (0.91,1.82)	0.161
Enlisted Flyer	310	1.47 (0.87,2.49)	0.152
Enlisted Groundcrew	848	0.86 (0.59,1.27)	0.450

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	133	53 (39.8)	0.76 (0.64,0.90)	<0.001**
Medium	141	48 (34.0)		
High	140	29 (20.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
411	0.93 (0.75,1.16)	0.540

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for the composite skin-reaction index. Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,159	318 (27.4)		
Background RH	347	110 (31.7)	1.24 (0.95,1.61)	0.113
Low RH	203	84 (41.4)	1.86 (1.37,2.53)	<0.001**
High RH	211	46 (21.8)	0.73 (0.52,1.04)	0.084
Low plus High RH	414	130 (31.4)	1.16 (0.90,1.49)	0.255

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,150		
Background RH	344	1.01 (0.73,1.38)	0.969
Low RH	202	1.64 (1.14,2.37)	0.008**
High RH	209	0.91 (0.60,1.38)	0.658
Low plus High RH	411	1.22 (0.89,1.67)	0.219

[a]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
Low	257	82 (31.9)	0.92 (0.84,1.01)	0.091
Medium	249	93 (37.3)		
High	255	65 (25.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
755	1.05 (0.92,1.20)	0.438

[a]Relative risk for a twofold increase in 1987 dioxin.

10.2.2.2   *Laboratory Variable*

10.2.2.2.1   *PSA (Continuous)*

All results from the unadjusted and adjusted analyses of Models 1, 3, and 4 for the continuous form of PSA were nonsignificant (Table 10-37(a,b,e-h): p>0.06 for all analyses).

The unadjusted Model 2 analysis revealed a significant inverse association between initial dioxin and PSA as a continuous variable (Table 10-37(c): Slope=−0.064, p=0.027). After adjusting for covariates, the association was nonsignificant (Table 10-37(d): p=0.139).

Table 10-37. Analysis of PSA (ng/mL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*714*	*0.95*	*-0.02*	*0.644*
	Comparison	*1,089*	*0.97*		
Officer	Ranch Hand	274	0.98	-0.12	0.078
	Comparison	418	1.10		
Enlisted Flyer	Ranch Hand	117	1.12	0.10	0.318
	Comparison	171	1.02		
Enlisted Groundcrew	Ranch Hand	323	0.87	0.01	0.778
	Comparison	500	0.86		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value is based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*710*	*1.08*	*0.01*	*0.789*
	Comparison	*1,083*	*1.07*		
Officer	Ranch Hand	273	1.00	-0.10	0.151
	Comparison	418	1.10		
Enlisted Flyer	Ranch Hand	116	1.21	0.14	0.221
	Comparison	169	1.07		
Enlisted Groundcrew	Ranch Hand	321	1.09	0.07	0.263
	Comparison	496	1.02		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value is based on difference of means on natural logarithm scale.

Table 10-37. Analysis of PSA (ng/mL) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	123	1.16	1.15	0.034	-0.064 (0.029)	0.027*
Medium	130	0.86	0.85			
High	135	0.87	0.88			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of PSA versus log_2 (initial dioxin).

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	123	0.78	0.122	-0.049 (0.033)	0.139
Medium	130	0.61			
High	133	0.62			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of PSA versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,089	0.97	0.97		
Background RH	325	0.96	0.94	-0.03	0.575
Low RH	187	1.06	1.07	0.10	0.129
High RH	201	0.85	0.86	-0.11	0.062
Low plus High RH	388	0.95	0.96	-0.01	0.781

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-37. Analysis of PSA (ng/mL) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,083	1.07		
Background RH	323	1.02	-0.05	0.429
Low RH	187	1.18	0.11	0.159
High RH	199	1.10	0.03	0.660
Low plus High RH	386	1.14	0.07	0.256

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value is based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	242	1.00	0.004	-0.029 (0.018)	0.113
Medium	229	1.02			
High	242	0.85			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of PSA versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	241	0.93	0.069	-0.008 (0.021)	0.713
Medium	228	0.95			
High	240	0.84			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of PSA versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

10.2.2.2.2   PSA (Discrete)

There were no significant findings in the unadjusted and adjusted analyses of the discrete form of PSA for Models 1, 3, and 4 (Table 10-38(a,b,e-h): p>0.10 for all analyses).

The Model 2 unadjusted analysis of the discrete form of PSA revealed a significant inverse relation between initial dioxin and discrete PSA levels (Table 10-38(c): Unadjusted RR=0.58, p=0.013). After covariate adjustment, the result was no longer significant (Table 10-38(d): p=0.058).

Table 10-38. Analysis of PSA (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*714*	*32 (4.5)*	*0.83 (0.54,1.30)*	*0.418*
	Comparison	*1,089*	*58 (5.3)*		
Officer	Ranch Hand	274	18 (6.6)	0.94 (0.51,1.73)	0.851
	Comparison	418	29 (6.9)		
Enlisted Flyer	Ranch Hand	117	5 (4.3)	0.72 (0.24,2.16)	0.556
	Comparison	171	10 (5.8)		
Enlisted Groundcrew	Ranch Hand	323	9 (2.8)	0.73 (0.32,1.62)	0.435
	Comparison	500	19 (3.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,793*	*1.07 (0.62,1.86)*	*0.800*
Officer	691	1.19 (0.60,2.35)	0.621
Enlisted Flyer	285	0.98 (0.30,3.16)	0.967
Enlisted Groundcrew	817	0.94 (0.39,2.27)	0.887

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	123	11 (8.9)	0.58 (0.35,0.93)	0.013*
Medium	130	4 (3.1)		
High	135	2 (1.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 10-38. Analysis of PSA (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
386	0.60 (0.34,1.06)	0.058

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	**n**	**Number (%) High**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Comparison	1,089	58 (5.3)		
Background RH	325	15 (4.6)	0.84 (0.47,1.51)	0.566
Low RH	187	12 (6.4)	1.23 (0.64,2.33)	0.534
High RH	201	5 (2.5)	0.46 (0.18,1.17)	0.103
Low plus High RH	388	17 (4.4)	0.74 (0.40,1.35)	0.326

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,083		
Background RH	323	0.91 (0.46,1.77)	0.773
Low RH	187	1.57 (0.75,3.30)	0.230
High RH	199	0.95 (0.34,2.69)	0.926
Low plus High RH	386	1.21 (0.59,2.48)	0.596

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 10-38. Analysis of PSA (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	242	13 (5.4)	0.84 (0.67,1.05)	0.115
Medium	229	13 (5.7)		
High	242	6 (2.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
709	1.02 (0.76,1.38)	0.874

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for cumulative herbicide exposure because of the sparse number of Ranch Hands who did not report herbicide exposure.

10.3 DISCUSSION

The 2002 follow-up examination of the AFHS combined physical examination, interval history, and laboratory evaluation to assess the risk of benign and malignant neoplasia to study participants exposed to herbicides (Ranch Hands) compared to matched controls who were not exposed (Comparisons). Data collected at the 2002 follow-up examination were added to data from earlier assessments and a cancer history for each participant who attended the 2002 follow-up examination was created.

Although exposure to herbicides has been determined to be carcinogenic in animal studies, the exposure required for malignant transformation of normal cells and the types of tumors produced are species-dependent. Therefore, while animal studies provide conclusive evidence on the carcinogenic potential of dioxin, the determination of causality in humans remains to be established. Many studies have assessed the carcinogenic potential of dioxin in humans (43-183), as described previously in this chapter (see Section 10.1.1.3). While the cumulative data from these studies have not been entirely consistent, there does appear to be an association between dioxin exposure in humans and an increased risk of developing cancers of the skin, lung, bladder, kidney, connective tissue, and lymphatic system. Part of the apparent inconsistencies may be due to significant differences in cumulative dose, dose-rate (one-time acute exposure versus chronic, low-dose exposure), frequency of assessments, and confounding risk factors or unaccounted exposure to co-promoters or co-carcinogens (e.g., tobacco smoke, either direct or second-hand).

As anticipated, there were several significant dependent variable-covariate associations that emerged from the 2002 data, including a strong association between age and the likelihood of developing most cancers. This association mirrors that seen in the general U.S. population.

Officers, the oldest participants on average, had a higher prevalence of skin cancer, primarily basal cell carcinoma, as well as the highest prevalence of cancer of any type. The prevalence of prostate cancer and abnormally high PSA results and the highest average levels of PSA were greater for officers and enlisted flyers. Enlisted flyers had the highest average PSA levels, while officers had the highest prevalence of abnormal PSA results.

Cancer prevalence was established by medical records review. For chest x-ray findings that were reported as needing follow-up at the 2002 physical examination, the AFHS made every effort to contact and to encourage participants to see their physicians. The participants were recontacted to determine a final diagnosis. Medical records review was accomplished to confirm reported neoplasms and to identify any unreported neoplasms. During physical examinations, newly discovered and suspicious skin lesions were biopsied if the study participant consented. A skin biopsy was indicated for 307 of the 1,951 (15.7%) participants at the 2002 follow-up examination; 289 of these 307 participants (94.1%) consented to the biopsy.

Several associations emerged. For example, there was an increased prevalence of skin cancers in the Ranch Hand cohort when compared against the Comparison cohort (54.2% versus 47.8%, respectively). This difference was further isolated to malignant skin cancer and, in particular, basal cell carcinoma. No significant associations between squamous cell carcinoma or melanoma and herbicide exposure were found. Although Ranch Hands exhibited an increased prevalence of basal cell carcinoma, the association was seen primarily in officers, who, on average, had the lowest dioxin levels. Higher prevalences were also observed in the Ranch Hand subgroups with the lowest levels of initial or 1987 dioxin. A higher percentage of the Ranch Hand cohort also exhibited skin cancers of uncertain behavior or unspecified nature. Again, there appeared to be an inverse correlation between dioxin and development of skin cancers, with the prevalence decreasing as dioxin increased. In summary, the data from this study did not support a dose-response relation between dioxin levels and development of nonmelanoma skin cancers.

Ranch Hands in the low dioxin category had an increased risk of bronchus and lung cancer relative to Comparisons. No trend of an increasing risk with increasing levels of dioxin was evident in the other analyses, however, and the available data from this study did not support a dose-response relation between dioxin levels and the development of lung cancer.

Ranch Hand officers had higher prevalence of colorectal and urinary system cancers. Colorectal cancer in the Ranch Hand low dioxin category and urinary system cancers in the Ranch Hand background dioxin category were increased. No increases in Ranch Hand high dioxin category were observed. These increases were based on fewer than 10 cases per exposure category.

Ranch Hands in the low dioxin category appeared to have an increased risk of developing prostate cancer relative to Comparisons. No association was found between PSA levels and levels of dioxin.

Ranch Hands in the low initial dioxin cohort had an increased risk of skin and systemic neoplasms combined, which reflects the skin neoplasm analyses discussed previously.

In summary, most associations between dioxin levels and cancer were found in the low Ranch Hand dioxin category. Further inferences are limited because of a small number of cancers in this low exposure group. Some of these associations may also be due to chance or lack of adjustment for a factor not

considered in these analyses. The group of Ranch Hands in the low dioxin category may merit additional study to ascertain the cause(s) of their malignancies, but the small size of the cohort and low actual numbers of events may make any additional conclusions difficult.

10.4 SUMMARY

A neoplasia history for each participant who attended the 2002 follow-up examination was developed by combining data from the 2002 follow-up examination with information collected at previous AFHS examinations and verifying the results through a review of medical records. In addition, PSA levels, as determined by the Scripps Clinic laboratory, were analyzed. Associations with herbicide exposure (i.e., group − Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable in the neoplasia assessment. The significant adjusted results are discussed in the sections below.

10.4.1 Model 1: Group Analysis

More Ranch Hands had skin neoplasms, basal cell carcinoma, nonmelanoma, and malignant systemic neoplasms of the urinary system than Comparisons in the overall analyses. When stratified by military occupation, Ranch Hand officers had an increased risk of basal cell carcinoma and, consequently, nonmelanoma skin cancers. Ranch Hand officers also had an increased risk of malignant systemic neoplasms and malignant systemic neoplasms of the colon and rectum and of the urinary system. No results were significant in the adjusted analyses of skin or systemic neoplasms for enlisted flyers or enlisted groundcrew. The results of the group analysis are provided in Table 10-39.

Table 10-39. Summary of Group Analysis (Model 1) for Neoplasia Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Skin Neoplasms				
All (D)	p=0.007 (1.29)	NS	NS	NS
Malignant (D)	NS	NS	NS	NS
Benign (D)	NS	NS	NS	NS
Uncertain Behavior or Unspecified Nature (D)	NS	NS	--	NS
Malignant: Basal Cell Carcinoma (D)	p=0.017 (1.34)	p=0.006 (1.62)	NS	ns
Malignant: Squamous Cell Carcinoma (D)	NS	NS	NS	NS
Malignant: Nonmelanoma (D)	p=0.019 (1.31)	p=0.019 (1.49)	NS	ns
Malignant: Melanoma (D)	ns	ns	ns	NS
Systemic Neoplasms				
All (D)	NS	NS	NS	NS
Malignant (D)	NS	p=0.023 (1.63)	NS	ns
Benign (D)	NS	ns	ns	NS
Uncertain Behavior or Unspecified Nature (D)	ns	ns	NS	ns
Malignant: Eye, Ear, Face, Head, and Neck (D)	ns	ns	NS	ns
Malignant: Oral Cavity, Pharynx, and Larynx (D)	ns	ns	NS	ns
Malignant: Thymus, Heart, and Mediastinum (D)	NS	NS	ns	NS
Malignant: Thyroid Gland (D)	ns	NS	--	ns
Malignant: Bronchus and Lung (D)	p=0.021 (2.86)	NS	NS	NS

	UNADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
All: Stomach (D)	NS	ns	NS	NS
Malignant: Colon and Rectum (D)	NS	p=0.037 (4.15)	ns	NS
Malignant: Urinary System (D)	p=0.023 (2.32)	NS	NS	NS
Malignant: Kidney and Ureter (D)	NS	NS	NS	NS
Malignant: Prostate (D)	NS	NS	NS	ns
Malignant: Penis and Other Male Genital Organs (D)	NS	--	NS	--
Malignant: Testicles (D)	NS	NS	NS	NS
Malignant: Bone and Articular Cartilage (D)	ns	ns	ns	ns
Malignant: Connective and Other Soft Tissues (D)	ns	ns	NS	ns
Malignant: Carcinoma in Situ (D)	NS	NS	ns	ns
Malignant: Hodgkin's Disease (D)	NS	NS	--	ns
Malignant: Leukemia (D)	NS	NS	NS	ns
Malignant: Lymphoid and Histiocytic Tissue (D)	NS	NS	ns	NS
Malignant: Lymphoreticular Sarcoma (D)	ns	ns	--	--
Skin and Systemic Neoplasms				
All (D)	p=0.042 (1.22)	NS	NS	NS
Malignant (D)	p=0.049 (1.22)	p=0.027 (1.41)	NS	ns
Laboratory				
PSA (C)	ns	ns	NS	NS
PSA (D)	ns	ns	ns	ns

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

      The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable.

      A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

	ADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Medical Records				
Skin Neoplasms				
All (D)	p=0.012 (1.28)	NS	NS	NS
Malignant (D)	NS	NS	NS	NS
Benign (D)	NS	NS	NS	NS
Uncertain Behavior or Unspecified Nature (D)	NS	NS	--	NS
Malignant: Basal Cell Carcinoma (D)	p=0.027 (1.33)	p=0.013 (1.58)	NS	NS
Malignant: Squamous Cell Carcinoma (D)	NS	ns	NS	NS
Malignant: Nonmelanoma (D)	p=0.027 (1.31)	p=0.032 (1.46)	NS	NS
Malignant: Melanoma (D)	ns	NS	ns	NS

	ADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Systemic Neoplasms				
All (D)	NS	NS	NS	ns
Malignant (D)	NS	p=0.014 (1.81)	NS	ns
Benign (D)	ns	ns	ns	NS
Uncertain Behavior or Unspecified Nature (D)	ns	ns	NS	ns
Malignant: Eye, Ear, Face, Head, and Neck (D)	ns	--	NS	--
Malignant: Oral Cavity, Pharynx, and Larynx (D)	ns	ns	NS	--
Malignant: Thymus, Heart, and Mediastinum (D)	NS	--	--	--
Malignant: Thyroid Gland (D)	ns	NS	--	--
Malignant: Bronchus and Lung (D)	NS	NS	NS	NS
All: Stomach (D)	ns	ns	NS	NS
Malignant: Colon and Rectum (D)	NS	p=0.044 (4.66)	ns	NS
Malignant: Urinary System (D)	p=0.018 (3.02)	p=0.049 (3.59)	NS	NS
Malignant: Kidney and Ureter (D)	NS	NS	--	NS
Malignant: Prostate (D)	NS	NS	NS	ns
Malignant: Penis and Other Male Genital Organs (D)	--	--	--	--
Malignant: Testicles (D)	--	--	--	--
Malignant: Bone and Articular Cartilage (D)	--	--	--	--
Malignant: Connective and Other Soft Tissues (D)	ns	--	NS	--
Malignant: Carcinoma in Situ (D)	NS	NS	NS	--
Malignant: Hodgkin's Disease (D)	NS	--	--	--
Malignant: Leukemia (D)	NS	NS	--	--
Malignant: Lymphoid and Histiocytic Tissue (D)	ns	NS	ns	ns
Malignant: Lymphoreticular Sarcoma (D)	ns	ns	--	--
Skin and Systemic Neoplasms				
All (D)	NS	NS	NS	NS
Malignant (D)	NS	NS	NS	ns
Laboratory				
PSA (C)	NS	ns	NS	NS
PSA (D)	NS	NS	ns	ns

--: The analysis was not performed because of the sparse number of participants with a neoplasm.

Note: NS or ns: Not significant (p>0.05).
   C: Continuous form of dependent variable.
   D: Discrete form of dependent variable.

   The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable.

   A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

10.4.2 Model 2: Initial Dioxin Analysis

As initial dioxin in Ranch Hands increased, the occurrence of skin neoplasms of uncertain behavior or unspecified nature decreased, as did the prevalence of a malignant neoplasm of the oral cavity, pharynx, or larynx. The prevalence of a malignant systemic neoplasm of the urinary system, however, increased as initial dioxin increased. The results of all unadjusted and adjusted Model 2 analyses are summarized in Table 10-40.

Table 10-40. Summary of Initial Dioxin Analysis (Model 2) for Neoplasia Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Skin Neoplasms		
All (D)	p=0.011 (0.82)	ns
Malignant (D)	p=0.021 (0.81)	ns
Benign (D)	ns	ns
Uncertain Behavior or Unspecified Nature (D)	p=0.018 (0.25)	p=0.033 (0.23)
Malignant: Basal Cell Carcinoma (D)	p=0.001 (0.72)	ns
Malignant: Squamous Cell Carcinoma (D)	ns	ns
Malignant: Nonmelanoma (D)	p=0.005 (0.77)	ns
Malignant: Melanoma (D)	ns	NS
Systemic Neoplasms		
All (D)	ns	ns
Malignant (D)	p=0.001 (0.69)	ns
Benign (D)	NS	ns
Uncertain Behavior or Unspecified Nature (D)	ns	NS
Malignant: Eye, Ear, Face, Head, and Neck (D)	NS	NS
Malignant: Oral Cavity, Pharynx, and Larynx (D)	p=0.017 (0.21)	p=0.010 (0.12)
Malignant: Thymus, Heart, and Mediastinum (D)	--	--
Malignant: Thyroid Gland (D)	ns	ns
Malignant: Bronchus and Lung (D)	ns	ns
All: Stomach (D)	NS	NS
Malignant: Colon and Rectum (D)	ns	NS
Malignant: Urinary System (D)	NS	p=0.049 (2.08)
Malignant: Kidney and Ureter (D)	NS	NS
Malignant: Prostate (D)	p<0.001 (0.54)	ns
Malignant: Penis and Other Male Genital Organs (D)	NS	NS
Malignant: Testicles (D)	ns	ns
Malignant: Bone and Articular Cartilage (D)	--	--
Malignant: Connective and Other Soft Tissues (D)	NS	NS
Malignant: Carcinoma in Situ (D)	ns	ns
Malignant: Hodgkin's Disease (D)	--	--
Malignant: Leukemia (D)	--	--
Malignant: Lymphoid and Histiocytic Tissue (D)	ns	ns
Malignant: Lymphoreticular Sarcoma (D)	--	--

Variable	Unadjusted	Adjusted
Skin and Systemic Neoplasms		
All (D)	p=0.011 (0.82)	ns
Malignant (D)	p<0.001 (0.76)	ns
Laboratory		
PSA (C)	p=0.027 (-0.064)	ns
PSA (D)	p=0.013 (0.58)	ns

--: The analysis was not performed because of the sparse number of Ranch Hands with a neoplasm.

Note: NS or ns: Not significant (p>0.05).
   C: Continuous form of dependent variable.
   D: Discrete form of dependent variable.

   The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

   A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

10.4.3 Model 3: Categorized Dioxin Analysis

The significant results of the Model 3 analyses were primarily found when comparing Ranch Hands in the low dioxin category with Comparisons. Ranch Hands in the low dioxin category had an increased risk of a basal cell carcinoma. This pattern was also seen in nonmelanoma skin cancers, malignant skin cancers, and all skin neoplasms (benign, malignant, and uncertain behavior). The risk of a skin neoplasm of uncertain behavior or unspecified nature was also increased for Ranch Hands in the low dioxin category.

The prevalence of a malignant systemic neoplasm, combined across sites, also was significantly increased for Ranch Hands in the low dioxin category relative to Comparisons. Significant results for the site-specific analyses included increased risks to Ranch Hands in the low dioxin category for malignant systemic neoplasms of the bronchus or lung, colon or rectum, prostate, and carcinoma in situ. These findings led to an increased risk for low Ranch Hands for all neoplasms and all malignant neoplasms (combining skin and systemic).

Ranch Hands in the background category had an increased risk of a malignant systemic neoplasm of the urinary system. Ranch Hands in the low and high dioxin categories combined had an increased prevalence of a skin neoplasm of any type. No significant results were found for Ranch Hands in the high dioxin category. The complete results of all unadjusted and adjusted Model 3 analyses are summarized in Table 10-41.

Table 10-41. Summary of Categorized Dioxin Analysis (Model 3) for Neoplasia Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
	Medical Records			
Skin Neoplasms				
All (D)	p=0.035 (1.31)	p=0.001 (1.69)	ns	p=0.037 (1.28)
Malignant (D)	NS	p=0.004 (1.66)	ns	NS
Benign (D)	NS	NS	NS	NS
Uncertain Behavior or Unspecified Nature (D)	NS	p=0.026 (4.51)	ns	NS
Malignant: Basal Cell Carcinoma (D)	p=0.012 (1.47)	p=0.002 (1.78)	ns	NS
Malignant: Squamous Cell Carcinoma (D)	NS	NS	ns	NS
Malignant: Nonmelanoma (D)	p=0.018 (1.42)	p=0.002 (1.73)	ns	NS
Malignant: Melanoma (D)	ns	NS	ns	ns
Systemic Neoplasms				
All (D)	NS	p=0.033 (1.39)	ns	NS
Malignant (D)	NS	p<0.001 (2.15)	ns	NS
Benign (D)	NS	NS	ns	ns
Uncertain Behavior or Unspecified Nature (D)	NS	NS	ns	ns
Malignant: Eye, Ear, Face, Head, and Neck (D)	ns	ns	NS	ns
Malignant: Oral Cavity, Pharynx, and Larynx (D)	ns	NS	ns	NS
Malignant: Thymus, Heart, and Mediastinum (D)	NS	ns	ns	ns
Malignant: Thyroid Gland (D)	ns	NS	ns	NS
Malignant: Bronchus and Lung (D)	NS	p<0.001 (6.43)	NS	p=0.047 (3.01)
All: Stomach (D)	NS	NS	ns	ns
Malignant: Colon and Rectum (D)	NS	p=0.009 (3.74)	ns	NS
Malignant: Urinary System (D)	p=0.023 (2.77)	p=0.042 (2.80)	NS	NS
Malignant: Kidney and Ureter (D)	NS	NS	NS	NS
Malignant: Prostate (D)	NS	p=0.007 (2.00)	ns	NS
Malignant: Penis and Other Male Genital Organs (D)	--	--	p=0.019 (*)	NS
Malignant: Testicles (D)	--	p=0.017 (*)	NS	p=0.025 (**)
Malignant: Bone and Articular Cartilage (D)	ns	ns	ns	ns
Malignant: Connective and Other Soft Tissues (D)	ns	ns	ns	ns
Malignant: Carcinoma in Situ (D)	ns	NS	ns	NS
Malignant: Hodgkin's Disease (D)	NS	ns	ns	ns
Malignant: Leukemia (D)	NS	ns	ns	ns
Malignant: Lymphoid and Histiocytic Tissue (D)	ns	NS	ns	NS
Malignant: Lymphoreticular Sarcoma (D)	ns	ns	ns	ns

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Skin and Systemic Neoplasms				
All (D)	NS	p=0.001 (1.74)	ns	NS
Malignant (D)	NS	p<0.001 (1.86)	ns	NS
Laboratory				
PSA (C)	ns	NS	ns	ns
PSA (D)	ns	NS	ns	ns

--: The analysis was not performed because of the sparse number of participants with a neoplasm.

*: Relative risk could not be calculated. Two Ranch Hands and no Comparisons had a neoplasm at this site.

**: Relative risk could not be calculated. Three Ranch Hands and no Comparisons had a neoplasm at this site.

Note: NS or ns: Not significant ($p>0.05$).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

The p-value was given if $p \le 0.05$. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Skin Neoplasms				
All (D)	NS	p=0.007 (1.56)	NS	p=0.026 (1.32)
Malignant (D)	NS	p=0.024 (1.52)	NS	NS
Benign (D)	NS	NS	NS	NS
Uncertain Behavior or Unspecified Nature (D)	NS	p=0.041 (4.14)	--	--
Malignant: Basal Cell Carcinoma (D)	NS	p=0.010 (1.66)	NS	NS
Malignant: Squamous Cell Carcinoma (D)	ns	NS	NS	NS
Malignant: Nonmelanoma (D)	NS	p=0.013 (1.60)	NS	NS
Malignant: Melanoma (D)	ns	NS	NS	NS
Systemic Neoplasms				
All (D)	ns	NS	NS	NS
Malignant (D)	NS	p=0.003 (2.05)	NS	NS
Benign (D)	ns	ns	NS	NS
Uncertain Behavior or Unspecified Nature (D)	ns	ns	ns	ns
Malignant: Eye, Ear, Face, Head, and Neck (D)	--	--	ns	--

	ADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Malignant: Oral Cavity, Pharynx, and Larynx (D)	--	NS	--	--
Malignant: Thymus, Heart, and Mediastinum (D)	NS	--	--	--
Malignant: Thyroid Gland (D)	--	NS	--	--
Malignant: Bronchus and Lung (D)	NS	p=0.024 (3.91)	NS	NS
All: Stomach (D)	ns	ns	ns	ns
Malignant: Colon and Rectum (D)	NS	p=0.035 (3.74)	NS	NS
Malignant: Urinary System (D)	p=0.018 (3.62)	NS	NS	NS
Malignant: Kidney and Ureter (D)	NS	NS	NS	NS
Malignant: Prostate (D)	NS	p=0.048 (1.85)	NS	NS
Malignant: Penis and Other Male Genital Organs (D)	--	--	--	--
Malignant: Testicles (D)	--	--	--	--
Malignant: Bone and Articular Cartilage (D)	--	--	--	--
Malignant: Connective and Other Soft Tissues (D)	--	--	ns	--
Malignant: Carcinoma in Situ (D)	NS	p=0.027 (20.75)	--	--
Malignant: Hodgkin's Disease (D)	NS	--	--	--
Malignant: Leukemia (D)	NS	--	--	--
Malignant: Lymphoid and Histiocytic Tissue (D)	ns	NS	ns	ns
Malignant: Lymphoreticular Sarcoma (D)	NS	--	--	--
Skin and Systemic Neoplasms				
All (D)	NS	p=0.048 (1.46)	ns	NS
Malignant (D)	NS	p=0.008 (1.64)	ns	NS
Laboratory				
PSA (C)	ns	NS	NS	NS
PSA (D)	ns	NS	ns	NS

--: The analysis was not performed because of the sparse number of participants with a neoplasm.

Note: NS or ns: Not significant (p>0.05).

   C: Continuous form of dependent variable.

   D: Discrete form of dependent variable.

   The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable.

   A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

10.4.4 Model 4: 1987 Dioxin Level Analysis

As 1987 dioxin in Ranch Hands increased, the prevalence of a malignant systemic neoplasm of the penis or other male genital organs increased. As 1987 dioxin increased, however, the occurrence of a malignant systemic neoplasm of the thymus, heart, or mediastinum, the kidney or ureter, or leukemia decreased. All results for Model 4 unadjusted and adjusted analyses are summarized in Table 10-42.

Table 10-42. Summary of 1987 Dioxin Analysis (Model 4) for Neoplasia Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Skin Neoplasms		
All (D)	ns	NS
Malignant (D)	ns	NS
Benign (D)	ns	ns
Uncertain Behavior or Unspecified Nature (D)	ns	ns
Malignant: Basal Cell Carcinoma (D)	ns	ns
Malignant: Squamous Cell Carcinoma (D)	ns	NS
Malignant: Nonmelanoma (D)	ns	NS
Malignant: Melanoma (D)	NS	NS
Systemic Neoplasms		
All (D)	ns	NS
Malignant (D)	ns	NS
Benign (D)	NS	NS
Uncertain Behavior or Unspecified Nature (D)	ns	ns
Malignant: Eye, Ear, Face, Head, and Neck (D)	NS	NS
Malignant: Oral Cavity, Pharynx, and Larynx (D)	NS	NS
Malignant: Thymus, Heart, and Mediastinum (D)	p=0.038 (0.40)	p=0.009 (0.04)
Malignant: Thyroid Gland (D)	ns	ns
Malignant: Bronchus and Lung (D)	NS	NS
All: Stomach (D)	NS	NS
Malignant: Colon and Rectum (D)	NS	NS
Malignant: Urinary System (D)	ns	ns
Malignant: Kidney and Ureter (D)	ns	p=0.048 (0.55)
Malignant: Prostate (D)	ns	ns
Malignant: Penis and Other Male Genital Organs (D)	NS	p=0.017 (3.52)
Malignant: Testicles (D)	NS	NS
Malignant: Bone and Articular Cartilage (D)	--	--
Malignant: Connective and Other Soft Tissues (D)	NS	NS
Malignant: Carcinoma in Situ (D)	NS	NS
Malignant: Hodgkin's Disease (D)	ns	ns
Malignant: Leukemia (D)	p=0.008 (0.43)	p=0.004 (0.40)
Malignant: Lymphoid and Histiocytic Tissue (D)	ns	ns
Malignant: Lymphoreticular Sarcoma (D)	ns	NS
Skin and Systemic Neoplasms		
All (D)	ns	NS
Malignant (D)	ns	NS
Laboratory		
PSA (C)	ns	ns
PSA (D)	ns	NS

--: The analysis was not performed because of the sparse number of Ranch Hands with a neoplasm.

Note: NS or ns: Not significant (p>0.05).
        C: Continuous form of dependent variable.
        D: Discrete form of dependent variable.

        The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable.

        A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

10.4.5   Summary of Significant Results

Table 10-43 summarizes the significant results (p≤0.05) for the adjusted analyses that were performed for the neoplasia assessment. The dependent variable and its table reference are listed along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and is explained in footnotes.

Table 10-43. Summary of Results from Significant Adjusted Analyses in the Neoplasia Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Percent Abnormal	Note
All Skin Neoplasms (10-3)	1	RH vs. C, All	0.012	1.28 (1.06,1.56)	RH: 54.2% C: 47.8%	(a)
	3	Low RH vs. C	0.007	1.56 (1.13,2.17)	RH: 61.0% C: 47.8%	(b)
	3	Low plus High RH vs. C	0.026	1.32 (1.03,1.68)	RH: 54.2% C: 47.8%	(b)
Malignant Skin Neoplasms (10-4)	3	Low RH vs. C	0.024	1.52 (1.06,2.19)	RH: 31.6% C: 21.5%	(b)
Skin Neoplasms of Uncertain Behavior or Unspecified Nature (10-6)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.033	0.23 (0.04,1.38)	Low: 2.4% Medium: 0.8% High: 0.0%	(c)
	3	Low RH vs. C	0.041	4.14 (1.06,16.16)	RH: 2.1% C: 0.5%	(b)
Basal Cell Carcinoma (All Sites Combined) (10-7)	1	RH vs. C, All	0.027	1.33 (1.03,1.71)	RH: 21.4% C: 16.9%	(a)
	1	RH vs. C, Officer	0.013	1.58 (1.10,2.27)	RH: 28.0% C: 19.4%	(a)
	3	Low RH vs. C	0.010	1.66 (1.13,2.43)	RH: 26.7% C: 16.9%	(b)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Percent Abnormal	Note
Nonmelanoma (10-9)	1	RH vs. C, All	0.027	1.31 (1.03,1.67)	RH: 24.3% C: 19.6%	(a)
	1	RH vs. C, Officer	0.032	1.46 (1.03,2.07)	RH: 30.7% C: 23.0%	(a)
	3	Low RH vs. C	0.013	1.60 (1.10,2.31)	RH: 29.9% C: 19.6%	(b)
Malignant Systemic Neoplasms (10-12)	1	RH vs. C, Officer	0.014	1.81 (1.13,2.91)	RH: 16.6% C: 10.8%	(a)
	3	Low RH vs. C	0.003	2.05 (1.28,3.26)	RH: 19.4% C: 10.1%	(b)
Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx) (10-17)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.010	0.12 (0.01,1.09)	Low: 2.9% Medium: 0.0% High: 0.0%	(c)
Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum) (10-18)	4	All RH: 1987 Dioxin	0.009	0.04 (0.00,7.74)	Low: 0.8% Medium: 0.0% High: 0.0%	(d)
Malignant Systemic Neoplasms (Bronchus and Lung) (10-20)	3	Low RH vs. C	0.024	3.91 (1.20,12.74)	RH: 3.9% C: 0.6%	(b)
Malignant Systemic Neoplasms (Colon and Rectum) (10-22)	1	RH vs. C, Officer	0.044	4.66 (1.04,20.80)	RH: 2.6% C: 0.7%	(a)
	3	Low RH vs. C	0.035	3.74 (1.10,12.73)	RH: 3.4% C: 0.9%	(b)
Malignant Systemic Neoplasms (Urinary System) (10-23)	1	RH vs. C, All	0.018	3.02 (1.16,7.89)	RH: 2.3% C: 1.0%	(a)
	1	RH vs. C, Officer	0.049	3.59 (1.01,12.81)	RH: 2.6% C: 1.1%	(a)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.049	2.08 (0.99,4.37)	Low: 1.5% Medium: 2.8% High: 2.1%	(c)
	3	Background RH vs. C	0.018	3.62 (1.24,10.51)	RH: 2.6% C: 1.0%	(b)
Malignant Systemic Neoplasms (Kidney and Ureter (10-24)	4	All RH: 1987 Dioxin	0.048	0.55 (0.31,0.98)	Low: 1.2% Medium: 0.4% High: 1.2%	(d)
Malignant Systemic Neoplasms (Prostate) (10-25)	3	Low RH vs. C	0.048	1.85 (1.00,3.39)	RH: 10.7% C: 5.7%	(b)
Malignant Systemic Neoplasms (Penis and Other Male Genital) (10-26)	4	All RH: 1987 Dioxin	0.017	3.52 (1.04,11.91)	Low: 0.0% Medium: 0.0% High: 0.8%	(d)
Carcinoma in Situ (10-30)	3	Low RH vs. C	0.027	20.75 (1.40,307.55)	RH: 1.5% C: 0.5%	(b)
Leukemia (10-32)	4	All RH: 1987 Dioxin	0.004	0.40 (0.21,0.74)	Low: 1.2% Medium: 0.4% High: 0.0%	(d)
Skin and Systemic Neoplasms (10-35)	3	Low RH vs. C	0.048	1.46 (1.00,2.12)	RH: 73.8% C: 61.7%	(b)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Percent Abnormal	Note
Malignant Skin and Systemic Neoplasms (10-36)	3	Low RH vs. C	0.008	1.64 (1.14,2.37)	RH: 41.4% C: 27.4%	(b)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal is presented for each exposure group in contrast.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal is presented for each dioxin category in contrast.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal is presented for each of three initial dioxin categories.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal is presented for each of three 1987 dioxin categories.

Note: RH = Ranch Hand.
C = Comparison.

Model 2:   Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt).

Model 3:   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Model 4:   Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

10.5   CONCLUSION

During the 2002 health interview, each study participant was asked a series of questions on the occurrence of cancer since the date of his last health interview. The self-reported conditions were verified by a medical records review and combined with cancer information collected at previous AFHS examinations. For chest x-ray findings that were reported as needing follow-up at the 2002 physical examination, the AFHS made every effort to contact and encourage participants to see their physicians. The participants were recontacted to determine a final diagnosis. Some possible neoplastic conditions were discovered by the physicians at the physical examination. Contingent upon participant authorization, suspicious skin lesions were biopsied and the pathology determined; no other invasive procedures were used to detect systemic neoplasms.

Skin neoplasms were analyzed by behavior type and cell type. Systemic neoplasms were analyzed by behavior and anatomical site. All skin and systemic neoplasms and all malignant skin and systemic neoplasms also were analyzed. Analyses were conducted on prostate-specific antigen, which was used to detect prostate enlargement and prostate cancer.

Contrasts of Ranch Hands with Comparisons by military occupation showed significant results only for officers. Ranch Hand officers had an increased risk of basal cell carcinoma and, consequently, nonmelanoma skin cancers. Ranch Hand officers also had an increased risk of malignant systemic

neoplasms. The analysis of malignant systemic neoplasms of the colon and rectum and of the urinary system showed a greater risk for Ranch Hand officers.

The prevalence of a malignant systemic neoplasm of the urinary system increased as initial dioxin in Ranch Hands increased.

When comparing categorized levels of dioxin, significant results were primarily found when comparing Ranch Hands in the low dioxin category with Comparisons. Ranch Hands in the low dioxin category had an increased risk of a basal cell carcinoma and, consequently, this pattern was also seen in nonmelanoma skin cancers, malignant skin cancers, and skin neoplasms (benign, malignant, and uncertain behavior). The risk of a skin neoplasm of uncertain behavior or unspecified nature was also increased for Ranch Hands in the low dioxin category.

The prevalence of a malignant systemic neoplasm, combined across sites, also was significantly increased for Ranch Hands in the low dioxin category relative to Comparisons. Significant results for the site-specific analyses included increased risks to Ranch Hands in the low dioxin category for malignant systemic neoplasms of the bronchus or lung, colon or rectum, and prostate. These findings led to an increased risk for Ranch Hands in the low dioxin category for all neoplasms and all malignant neoplasms (combining skin and systemic). Ranch Hands in the background category had an increased risk of a malignant systemic neoplasm of the urinary system. Ranch Hands in the low and high dioxin categories combined had an increased prevalence of a skin neoplasm of any type.

In conclusion, the significant associations between herbicide exposure or dioxin levels and the likelihood of developing cancer were seen primarily for Ranch Hand officers and Ranch Hands in the low dioxin category, which were the lower-exposed subgroups, on average. Some of these associations also may have been due to chance or to a lack of adjustment for a factor not considered in these analyses.

REFERENCES

1. The American Cancer Society. 2001. Clinical oncology. R.E. Lenhard, R.T. Osteen, and T.S. Gansler, eds. American Cancer Society: Atlanta, GA.

2. Van Miller, J.P., J.J. Lalich, and J.R. Allen. 1977. Increased incidence of neoplasms in rats exposed to low levels of tetrachlorodibenzo-p-dioxin. *Chemosphere* 6:537-44.

3. Kociba, R.J., D.G. Keyes, J.E. Beyer, R.M. Carreon, C.E. Wade, D.A. Dittenber, R.P. Kalnins, L.E. Frauson, C.N. Park, S.D. Barnard, R.A. Hummel, and C.G. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicology and Applied Pharmacology* 46:279-303.

4. Toth, K., J. Sugar, S. Somfai-Relle, and J. Bence. 1978. Carcinogenic bioassay of the herbicide 2,4,5-trichlorophenoxyethanol (TCPE) with different 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) content in Swiss mice. *Progress in Biochemical Pharmacology* 14:82-93.

5. National Toxicology Program. 1982. Bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin for possible carcinogenicity (Gavage study). *Technical Report Series* No. 209. Research Triangle Park, NC.

6. National Toxicology Program. 1982. Carcinogenesis bioassay of 2,3,7,8-tetrachlorodibenzo-p-dioxin (CAS no. 1746-01-6) in Swiss-Webster mice (dermal study). Report 80-32. NIH publication no. 82-1757. *Technical Report Series* No. 201. Research Triangle Park, NC.

7. Della Porta, G., T.A. Dragani, and G. Sozzi. 1987. Carcinogenic effects of infantile and long-term 2,3,7,8-tetrachlorodibenzo-p-dioxin treatment in the mouse. *Tumori* 73:99-107.

8. Rao, M.S., V. Subbarao, J.D. Prasad, and D.G. Scarpelli. 1988. Carcinogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the Syrian golden hamster. *Carcinogenesis* 9:1677-9.

9. DiGiovanni, J., A. Viaje, D.L. Berry, T.J. Slaga, and M.R. Juchau. 1977. Tumor-initiating ability of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and Arochlor 1254 in the two-stage system of mouse skin carcinogenesis. *Bulletin of Environmental Contamination and Toxicology* 18:552-7.

10. Scott, M.A., R.P. Tarara, A.G. Hendrickx, K. Benirschke, J.W. Overstreet, and B.L. Lasley. 2001. Exposure to the dioxin 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) induces squamous metaplasia in the endocervix of cynomolgus macaques. *Journal of Medical Primatology* 30:156-60.

11. Huff, J.E. 1992. 2,3,7,8-TCDD: A potent and complete carcinogen in experimental animals. *Chemosphere* 25:173-6.

12. Institute of Medicine. 2003. Veterans and Agent Orange: Update 2002. National Academy Press: Washington, DC.

13. Viluksela, M., Y. Bager, J.T. Tuomisto, G. Scheu, M. Unkila, R. Pohjanvirta, S. Flodstrom, V.M. Kosma, J. Maki-Paakkanen, T. Vartiainen, C. Klimm, K.W. Schramm, L. Warngard, and J. Tuomisto. 2000. Liver tumor-promoting activity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in TCDD-sensitive and TCDD-resistant rat strains. *Cancer Research* 60:6911-20.

14. Walker, N.J., A.M. Tritscher, R.C. Sills, G.W. Lucier, and C.J. Portier. 2000. Hepatocarcinogenesis in female Sprague-Dawley rats following discontinuous treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicological Sciences* 54:330-7.

15. Johnson, E.S. 1993. Important aspects of the evidence for TCDD carcinogenicity in man. *Environmental Health Perspectives* 99:383-90.

16. Okey, A.B., D.S. Riddick, and P.A. Harper. 1994. The Ah receptor: mediator of the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. *Toxicology Letters* 70:1-22.

17. Brown, M.M., T.L. McCready, and N.J. Bunce. 1992. Factors affecting the toxicity of dioxin-like toxicants: A molecular approach to risk assessment of dioxins. *Toxicology Letters* 61:141-7.

18. DeVito, M., T. Umbreit, T. Thomas, and M. Gallo. 1991. An analogy between the actions of the Ah receptor and the estrogen receptor for use in the biological basis for risk assessment of dioxin. In: Banbury Report 35: Biological Basis for Risk Assessment of Dioxins and Related Compounds. M.A. Gallo, R.J. Scheuplein, and K.A. van der Heijden, eds. Cold Spring Harbor Laboratory Press: Plainview, NY.

19. Safe, S. 1993. Development of bioassays and approaches for the risk assessment of 2,3,7,8-tetrachlorodibenzo-p-dioxin and related compounds. *Environmental Health Perspectives* 101(Suppl 3):317-25.

20. Andersen, M., and W. Greenlee. 1991. Biological determinants of TCDD pharmacokinetics and their relation to a biologically based risk assessment. In: Banbury Report 35: Biological Basis for Risk Assessment of Dioxins and Related Compounds. M.A. Gallo, R.J. Scheuplein, and K.A. van der Heijden, eds. Cold Spring Harbor Laboratory Press: Plainview, NY.

21. Rao, V.R. 1991. Molecular mechanism of action of dioxin-implications of its carcinogenic potency estimation. *Toxic Substances Journal* 8:335-51.

22. Houk, V.N. 1992. Review of research on health effects of PCDDs and PCDFs to develop human risk assessment. *Toxic Substances Journal* 12:181-90.

23. Kimbrough, R.D. 1992. Tolerable daily intake of 2,3,7,8-tetrachlorodibenzo-p-dioxin: Recent data on mechanism and animal carcinogenicity. *Toxic Substances Journal* 12:295-306.

24. Andersen, M.E., and R.B. Conolly. 1998. Mechanistic modeling of rodent liver tumor promotion at low levels of exposure: An example related to dose-response relationships for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Human and Experimental Toxicology* 17:683-90.

25. Grassman, J.A., S.A. Masten, N.J. Walker, and G.W. Lucier. 1998. Animal models of human response to dioxins. *Environmental Health Perspectives* 106(Suppl 2):761-75.

26. Dragan, Y.P., and D. Schrenk. 2000. Animal studies addressing the carcinogenicity of TCDD (or related compounds) with an emphasis on tumour promotion. *Food Additives and Contaminants* 17:289-302.

27. Wyde, M.E., V.A. Wong, A.H. Kim, G.W. Lucier, and N.J. Walker. 2001. Induction of hepatic 8-oxo-deoxyguanosine adducts by 2,3,7,8-tetrachlorodibenzo-p-dioxin in Sprague-Dawley rats is female-specific and estrogen-dependent. *Chemical Research in Toxicology* 14:849-55.

28. Schwarz, M., A. Buchmann, S. Stinchcombe, A. Kalkuhl, and K. Bock. 2000. Ah receptor ligands and tumor promotion: survival of neoplastic cells. *Toxicology Letters* 112-113:69-77.

29. Luebeck, E.G., A. Buchmann, S. Stinchcombe, S.H. Moolgavkar, and M. Schwarz. 2000. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on initiation and promotion of GST-P-positive foci in rat liver: A quantitative analysis of experimental data using a stochastic model. *Toxicology and Applied Pharmacology* 167:63-73.

30. Teeguarden, J.G., Y.P. Dragan, J. Singh, J. Vaughan, Y.H. Xu, T. Goldsworthy, and H.C. Pitot. 1999. Quantitative analysis of dose- and time-dependent promotion of four phenotypes of altered hepatic foci by 2,3,7,8-tetrachlorodibenzo-p-dioxin in female Sprague-Dawley rats. *Toxicological Sciences* 51:211-23.

31. Huff, J., G. Lucier, and A. Tritscher. 1994. Carcinogenicity of TCDD: Experimental, mechanistic, and epidemiologic evidence. *Annual Review of Pharmacology and Toxicology* 34:343-72.

32. Poland, A., and J.C. Knutson. 1982. 2,3,7,8-tetrachlorodibenzo-p-dioxin and related halogenated aromatic hydrocarbons: Examination of the mechanism of toxicity. *Annual Review of Pharmacology and Toxicology* 22:517-54.

33. Denison, M.S. 1992. Heterogeneity of rat hepatic Ah receptor: Identification of two receptor forms which differ in their biochemical properties. *Journal of Biochemical Toxicology* 7:249-56.

34. Lucier, G.W., C.J. Portier, and M.A. Gallo. 1993. Receptor mechanisms and dose-response models for the effects of dioxins. *Environmental Health Perspectives* 101:36-44.

35. Whitlock, J.P., Jr. 1990. Genetic and molecular aspects of 2,3,7,8-tetrachlorodibenzo-p-dioxin action. *Annual Review of Pharmacology and Toxicology* 30:251-77.

36. Silbergeld, E.K., and T.A. Gasiewicz. 1989. Dioxins and the Ah receptor. *American Journal of Industrial Medicine* 16:455-74.

37. Roberts, E.A., K.C. Johnson, P.A. Harper, and A.B. Okey. 1990. Characterization of the Ah receptor mediating aryl hydrocarbon hydroxylase induction in the human liver cell line Hep G2. *Archives of Biochemistry and Biophysics* 276:442-50.

38. Choi, E.J., D.G. Toscano, J.A. Ryan, N. Riedel, and W.A. Toscano, Jr. 1991. Dioxin induces transforming growth factor-alpha in human keratinocytes. *The Journal of Biological Chemistry* 266:9591-7.

39. Waithe, W.I., M. Michaud, P.A. Harper, A.B. Okey, and A. Anderson. 1991. The Ah receptor, cytochrome P450IA1 mRNA induction, and aryl hydrocarbon hydroxylase in a human lymphoblastoid cell line. *Biochemical Pharmacology* 41:85-92.

40. Lorenzen, A., and A.B. Okey. 1991. Detection and characterization of Ah receptor in tissue and cells from human tonsils. *Toxicology and Applied Pharmacology* 107:203-14.

41. Wang, X., M. Santostefano, Y. Lu, and S. Safe. 1992. A comparison of the mouse versus human aryl hydrocarbon (Ah) receptor complex: Effects of proteolysis. *Chemico-biological Interactions* 85:79-93.

42. Prokipcak, R.D., C.L. Golas, D.K. Manchester, A.B. Okey, S. Safe, and T. Fujita. 1990. 7-Substituted-2,3-dichlorodibenz-p-dioxins as competitive ligands for the Ah receptor: Quantitative structure activity relationship (QSARS) and a comparison of human receptor with Ah receptor from rodents. *Chemosphere* 20:1221-8.

43. Landi, M.T., P.A. Bertazzi, A. Baccarelli, D. Consonni, S. Masten, G. Lucier, P. Mocarelli, L. Needham, N. Caporaso, and J. Grassman. 2003. TCDD-mediated alterations in the AhR-dependent pathway in Seveso, Italy, 20 years after the accident. *Carcinogenesis* 24:673-80.

44. Bertazzi, P.A., A.C. Pesatori, I. Bernucci, M.T. Landi, and D. Consonni. 1999. Dioxin exposure and human leukemias and lymphomas. Lessons from the Seveso accident and studies on industrial workers. *Leukemia* 13(Suppl 1):S72-4.

45. Bertazzi, P.A., D. Consonni, S. Bachetti, M. Rubagotti, A. Baccarelli, C. Zocchetti, and A.C. Pesatori. 2001. Health effects of dioxin exposure: A 20-year mortality study. *American Journal of Epidemiology* 153:1031-44.

46. Bertazzi, A., A.C. Pesatori, D. Consonni, A. Tironi, M.T. Landi, and C. Zocchetti. 1993. Cancer incidence in a population accidentally exposed to 2,3,7,8-tetrachlorodibenzo-para-dioxin. *Epidemiology* 4:398-406.

47. Bertazzi, P.A., C. Zocchetti, A.C. Pesatori, S. Guercilena, M. Sanarico, and L. Radice. 1989. Ten-year mortality study of the population involved in the Seveso incident in 1976. *American Journal of Epidemiology* 129:1187-200.

48. Bertazzi, P.A., C. Zocchetti, S. Guercilena, D. Consonni, A. Tironi, M.T. Landi, and A.C. Pesatori. 1997. Dioxin exposure and cancer risk: A 15-year mortality study after the "Seveso accident." *Epidemiology* 8:646-52.

49. Bertazzi, P.A., I. Bernucci, G. Brambilla, D. Consonni, and A.C. Pesatori. 1998. The Seveso studies on early and long-term effects of dioxin exposure: A review. *Environmental Health Perspectives* 106(Suppl 2):625-33.

50. di Domenico, A., and G.A. Zapponi. 1986. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the environment: Human health risk estimation and its application to the Seveso case as an example. *Regulatory Toxicology and Pharmacology* 6:248-60.

51. Pesatori, A.C., D. Consonni, A. Tironi, C. Zocchetti, A. Fini, and P.A. Bertazzi. 1993. Cancer in a young population in a dioxin-contaminated area. *International Journal of Epidemiology* 22:1010-3.

52. Pesatori, A., D. Consonni, A. Tironi, M.T. Landi, C. Zocchetti, and P.A. Bertazzi. 1992. Cancer morbidity in the Seveso area, 1976-1986. *Chemosphere* 25:209-12.

53. Warner, M., B. Eskenazi, P. Mocarelli, P.M. Gerthoux, S. Samuels, L. Needham, D. Patterson, and P. Brambilla. 2002. Serum dioxin concentrations and breast cancer risk in the Seveso Women's Health Study. *Environmental Health Perspectives* 110:625-8.

54. Costani, G., P. Rabitti, A. Mambrini, E. Bai, and F. Berrino. 2000. Soft tissue sarcomas in the general population living near a chemical plant in Northern Italy. *Tumori* 86:381-3.

55. Ohta, S., S. Kuriyama, O. Aozasa, T. Nakao, M. Tanahashi, and H. Miyata. 2000. Survey on levels of PCDDs, PCDFs, and non-ortho Co-PCBs in soil and sediment from a high cancer area near a batch-type municipal solid waste incinerator in Japan. *Bulletin of Environmental Contamination and Toxicology* 64:630-7.

56. Revich, B., E. Aksel, T. Ushakova, I. Ivanova, N. Zhuchenko, N. Klyuev, B. Brodsky, and Y. Sotskov. 2001. Dioxin exposure and public health in Chapaevsk, Russia. *Chemosphere* 43:951-66.

57. Viel, J.F., P. Arveux, J. Baverel, and J.Y. Cahn. 2000. Soft-tissue sarcoma and non-Hodgkin's lymphoma clusters around a municipal solid waste incinerator with high dioxin emission levels. *American Journal of Epidemiology* 152:13-9.

58. Floret, N., F. Mauny, B. Challier, P. Arveux, J.Y. Cahn, and J.F. Viel. 2003. Dioxin emissions from a solid waste incinerator and risk of non-Hodgkin lymphoma. *Epidemiology* 14:392-8.

59. Pesatori, A.C., D. Consonni, S. Bachetti, C. Zocchetti, M. Bonzini, A. Baccarelli, and P.A. Bertazzi. 2003. Short- and long-term morbidity and mortality in the population exposed to dioxin after the "Seveso Accident." *Industrial Health* 41:127-38.

60. Becher, H., J. Wahrendorf, and R. Angerer. 1992. A cohort study on persons exposed to phenoxy acid herbicides and their contaminants in Germany—design and first results. *Chemosphere* 25:1007-14.

61. Becher, H., D. Flesch-Janys, T. Kauppinen, M. Kogevinas, K. Steindorf, A. Manz, and J. Wahrendorf. 1996. Cancer mortality in German male workers exposed to phenoxy herbicides and dioxins. *Cancer Causes and Control* 7:312-21.

62. Becher, H., K. Steindorf, and D. Flesch-Janys. 1998. Quantitative cancer risk assessment for dioxins using an occupational cohort. *Environmental Health Perspectives* 106(Suppl 2):663-70.

63. Bond, G.G., M.G. Ott, F.E. Brenner, and R.R. Cook. 1983. Medical and morbidity surveillance findings among employees potentially exposed to TCDD. *British Journal of Industrial Medicine* 40:318-24.

64. Bond, G.G., R.R. Cook, F.E. Brenner, and E.A. McLaren. 1987. Evaluation of mortality patterns among chemical workers with chloracne. *Chemosphere* 16:2117-21.

65. Bond, G.G., E.A. McLaren, T.E. Lipps, and R.R. Cook. 1989. Update of mortality among chemical workers with potential exposure to the higher chlorinated dioxins. *Journal of Occupational Medicine* 31:121-3.

66. Bueno de Mesquita, H.B., G. Doornbos, D.A. van der Kuip, M. Kogevinas, and R. Winkelmann. 1993. Occupational exposure to phenoxy herbicides and chlorophenols and cancer mortality in The Netherlands. *American Journal of Industrial Medicine* 23:289-300.

67. Buffler, P.A., S.M. Wood, L. Suarez, and D.J. Kilian. 1978. Mortality follow-up of workers exposed to 1,4-dioxane. *Journal of Occupational Medicine* 20:255-9.

68. Coggon, D., B. Pannett, and P. Winter. 1991. Mortality and incidence of cancer at four factories making phenoxy herbicides. *British Journal of Industrial Medicine* 48:173-8.

69. Collins, J.J., M.E. Strauss, G.J. Levinskas, and P.R. Conner. 1993. The mortality experience of workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin in a trichlorophenol process accident. *Epidemiology* 4:7-13.

70. Cook, R.R., J.C. Townsend, M.G. Ott, and L.G. Silverstein. 1980. Mortality experience of employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Journal of Occupational Medicine* 22:530-2.

71. Cook, R.R., G.G. Bond, R.A. Olson, M.G. Ott, and M.R. Gondek. 1986. Evaluation of the mortality experience of workers exposed to the chlorinated dioxins. *Chemosphere* 15:1769-76.

72. Cook, R.R., G.G. Bond, R.A. Olson, and M.G. Ott. 1987. Update of the mortality experience of workers exposed to chlorinated dioxins. *Chemosphere* 16:2111-6.

73. Dalderup, L.M., and D. Zellenrath. 1983. Dioxin exposure: 20 year follow-up. *Lancet* 2:1134-5.

74. Fingerhut, M.A., W.E. Halperin, D.A. Marlow, L.A. Piacitelli, P.A. Honchar, M.H. Sweeney, A.L. Greife, P.A. Dill, K. Steenland, and A.J. Suruda. 1991. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324:212-8.

75. Fitzgerald, E.F., A.L. Weinstein, L.G. Youngblood, S.J. Standfast, and J.M. Melius. 1989. Health effects three years after potential exposure to the toxic contaminants of an electrical transformer fire. *Archives of Environmental Health* 44:214-21.

76. Flesch-Janys, D., J. Berger, J. Konietzko, A. Manz, S. Nagel, and J. Wahrendorf. 1992. Quantification of exposure to dioxins and furans in a cohort of workers of a herbicide producing plant in Hamburg, FRG. *Chemosphere* 25:1021-7.

77. Flesch-Janys, D., J. Berger, P. Gurn, A. Manz, S. Nagel, H. Waltsgott, and J.H. Dwyer. 1995. Exposure to polychlorinated dioxins and furans (PCDD/F) and mortality in a cohort of workers from a herbicide-producing plant in Hamburg, Federal Republic of Germany. *American Journal of Epidemiology* 142:1165-75.

78. Flesch-Janys, D., K. Steindorf, P. Gurn, and H. Becher. 1998. Estimation of the cumulated exposure to polychlorinated dibenzo-p-dioxins/furans and standardized mortality ratio analysis of cancer mortality by dose in an occupationally exposed cohort. *Environmental Health Perspectives* 106(Suppl 2):655-62.

79. Hooiveld, M., D.J. Heederik, M. Kogevinas, P. Boffetta, L.L. Needham, D.G. Patterson, Jr., and H.B. Bueno-de-Mesquita. 1998. Second follow-up of a Dutch cohort occupationally exposed to phenoxy herbicides, chlorophenols, and contaminants. *American Journal of Epidemiology* 147:891-901.

80. Kogevinas, M., H. Becher, T. Benn, P.A. Bertazzi, P. Boffetta, H.B. Bueno-de-Mesquita, D. Coggon, D. Colin, D. Flesch-Janys, M. Fingerhut, L. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, N. Pearce, and R. Saracci. 1997. Cancer mortality in workers exposed to phenoxy herbicides, chlorophenols, and dioxins. An expanded and updated international cohort study. *American Journal of Epidemiology* 145:1061-75.

81. Kogevinas, M., T. Kauppinen, R. Winkelmann, H. Becher, P.A. Bertazzi, H.B. Bueno-de-Mesquita, D. Coggon, L. Green, E. Johnson, M. Littorin, E. Lynge, D.A. Marlow, J.D. Mathews, M. Neuberger, T. Benn, B. Pannett, N. Pearce, and R. Saracci. 1995. Soft tissue sarcoma and non-Hodgkin's lymphoma in workers exposed to phenoxy herbicides, chlorophenols, and dioxins: Two nested case-control studies. *Epidemiology* 6:396-402.

82. Kogevinas, M., R. Saracci, R. Winkelmann, E.S. Johnson, P.A. Bertazzi, B.H. Bueno de Mesquita, T. Kauppinen, M. Littorin, E. Lynge, M. Neuberger. 1993. Cancer incidence and mortality in women occupationally exposed to chlorophenoxy herbicides, chlorophenols, and dioxins. *Cancer Causes and Control* 4:547-53.

83. Manz, A., J. Berger, J.H. Dwyer, D. Flesch-Janys, S. Nagel, and H. Waltsgott. 1991. Cancer mortality among workers in chemical plant contaminated with dioxin. *Lancet* 338:959-64.

84. May, G. 1982. Tetrachlorodibenzodioxin: A survey of subjects ten years after exposure. *British Journal of Industrial Medicine* 39:128-35.

85. Messerer, P., A. Zober, and H. Becher. 1998. Blood lipid concentrations of dioxins and furans in a sample of BASF employees included in the IARC registry of workers exposed to phenoxy acid herbicides and/or chlorophenols. *Environmental Health Perspectives* 106(Suppl 2):733-5.

86. Ott, M.G., B.B. Holder, and R.D. Olson. 1980. A mortality analysis of employees engaged in the manufacture of 2,4,5-trichlorophenoxyacetic acid. *Journal of Occupational Medicine* 22:47-50.

87. Ott, M.G., R.A. Olson, R.R. Cook, and G.G. Bond. 1987. Cohort mortality study of chemical workers with potential exposure to the higher chlorinated dioxins. *Journal of Occupational Medicine* 29:422-9.

88. Ott, M.G., and A. Zober. 1996. Cause specific mortality and cancer incidence among employees exposed to 2,3,7,8-TCDD after a 1953 reactor accident. *Occupational and Environmental Medicine* 53:606-12.

89. Ramlow, J.M., N.W. Spadacene, S.R. Hoag, B.A. Stafford, J.B. Cartmill, and P.J. Lerner. 1996. Mortality in a cohort of pentachlorophenol manufacturing workers, 1940-1989. *American Journal of Industrial Medicine* 30:180-94.

90. Saracci, R., M. Kogevinas, P.A. Bertazzi, B.H. Bueno de Mesquita, D. Coggon, L.M. Green, T. Kauppinen, K.A. L'Abbe, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, J. Osman, N. Pearce, and R. Winkelmann. 1991. Cancer mortality in workers exposed to chlorophenoxy herbicides and chlorophenols. *Lancet* 338:1027-32.

91. Steenland, K., J. Deddens, and L. Piacitelli. 2001. Risk assessment for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) based on an epidemiologic study. *American Journal of Epidemiology* 154:451-8.

92. Steenland, K., L. Piacitelli, J. Deddens, M. Fingerhut, and L.I. Chang. 1999. Cancer, heart disease, and diabetes in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of the National Cancer Institute* 91:779-86.

93. Thiess, A.M., R. Frentzel-Beyme, and R. Link. 1982. Mortality study of persons exposed to dioxin in a trichlorophenol-process accident that occurred in the BASF AG on November 17, 1953. *American Journal of Industrial Medicine* 3:179-89.

94. Thomas, T.L. 1987. Mortality among flavour and fragrance chemical plant workers in the United States. *British Journal of Industrial Medicine* 44:733-7.

95. Zack, J.A., and R.R. Suskind. 1980. The mortality experience of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident. *Journal of Occupational Medicine* 22:11-4.

96. Zober, A., and O. Papke. 1993. Concentrations of PCDDs and PCDFs in human tissue 36 years after accidental dioxin exposure. *Chemosphere* 27:413-8.

97. Zober, A., P. Messerer, and P. Huber. 1990. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. *International Archives of Occupational and Environmental Health* 62:139-57.

98. Zober, A., M.G. Ott, and P. Messerer. 1994. Morbidity follow up study of BASF employees exposed to 2,3,7, 8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

99. Asp, S., V. Riihimaki, S. Hernberg, and E. Pukkala. 1994. Mortality and cancer morbidity of Finnish chlorophenoxy herbicide applicators: An 18-year prospective follow-up. *American Journal of Industrial Medicine* 26:243-53.

100. Smith, A.H., D.G. Patterson, Jr., M.L. Warner, R. MacKenzie, and L.L. Needham. 1992. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin levels of New Zealand pesticide applicators and their implication for cancer hypotheses. *Journal of the National Cancer Institute* 84:104-8.

101. Lynge, E. 1985. A follow-up study of cancer incidence among workers in manufacture of phenoxy herbicides in Denmark. *British Journal of Cancer* 52:259-70.

102. Lynge, E. 1993. Cancer in phenoxy herbicide manufacturing workers in Denmark, 1947-87—an update. *Cancer Causes and Control* 4:261-72.

103. Coggon, D., B. Pannett, P.D. Winter, E.D. Acheson, and J. Bonsall. 1986. Mortality of workers exposed to 2 methyl-4 chlorophenoxyacetic acid. *Scandinavian Journal of Work, Environment and Health* 12:448-54.

104. Zack, J.A., and W.R. Gaffey. 1983. A mortality study of workers employed at the Monsanto company plant in Nitro, West Virginia. *Environmental Science Research* 26:575-91.

105. Petrelli, G., F. Menniti Ippolito, S. Spila Alegiani, G. Magarotto, and F. Taroni. 1994. Mortality among workers of three thermoelectric power plants in northern Italy: A retrospective cohort study. *Medicina del Lavoro* 85:397-401.

106. Boder, K.M., J.J. Collins, L.J. Bloemen, M.L. Carson. 2003. Cancer risk for chemical workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Occupational and Environmental Medicine* 60:672-75.

107. Steenland, K., and J. Deddens. 2003. Dioxin: Expose-response analyses and risk assessment. *Industrial Health* 41:175-80.

108. Bullman, T.A., K.K. Watanabe, and H.K. Kang. 1994. Risk of testicular cancer associated with surrogate measures of Agent Orange exposure among Vietnam veterans on the Agent Orange Registry. *Annals of Epidemiology* 4:11-6.

109. Clapp, R.W. 1997. Update of cancer surveillance of veterans in Massachusetts, USA. *International Journal of Epidemiology* 26:679-81.

110. Cordier, S., T.B. Le, P. Verger, D. Bard, C.D. Le, B. Larouze, M.C. Dazza, T.Q. Hoang, and L. Abenhaim. 1993. Viral infections and chemical exposures as risk factors for hepatocellular carcinoma in Vietnam. *International Journal of Cancer* 55:196-201.

111. Dalager, N.A., H.K. Kang, V.L. Burt, and L. Weatherbee. 1995. Hodgkin's disease and Vietnam service. *Annals of Epidemiology* 5:400-6.

112. Dalager, N.A., H.K. Kang, V.L. Burt, and L. Weatherbee. 1991. Non-Hodgkin's lymphoma among Vietnam veterans. *Journal of Occupational Medicine* 33:774-9.

113. Fett, M.J., J.R. Nairn, D.M. Cobbin, and M.A. Adena. 1987. Mortality among Australian conscripts of the Vietnam conflict era. II. Causes of death. *American Journal of Epidemiology* 125:878-84.

114. Irey, N.S., F.G. Mullick, and W.D. Foster. 1989. A morphologic study of Vietnam veterans. *Modern Pathology* 2:360-4.

115. Ketchum, N.S., J.E. Michalek, and J.E. Burton. 1999. Serum dioxin and cancer in veterans of Operation Ranch Hand. *American Journal of Epidemiology* 149:630-9.

116. Mahan, C.M., T.A. Bullman, H.K. Kang, and S. Selvin. 1997. A case-control study of lung cancer among Vietnam veterans. *Journal of Occupational and Environmental Medicine* 39:740-7.

117. Michalek, J.E., W.H. Wolfe, and J.C. Miner. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. II. Mortality. *Journal of the American Medical Association* 264:1832-6.

118. Michalek, J.E., N.S. Ketchum, and F.Z. Akhtar. 1998. Postservice mortality of US Air Force veterans occupationally exposed to herbicides in Vietnam: 15-year follow-up. *American Journal of Epidemiology* 148:786-92.

119. O'Brien, T.R., P. Decoufle, and C.A. Boyle. 1991. Non-Hodgkin's lymphoma in a cohort of Vietnam veterans. *American Journal of Public Health* 81:758-60.

120. Thomas, T.L., and H.K. Kang. 1990. Mortality and morbidity among Army Chemical Corps Vietnam veterans: A preliminary report. *American Journal of Industrial Medicine* 18:665-73.

121. Watanabe, K.K., and H.K. Kang. 1995. Military service in Vietnam and the risk of death from trauma and selected cancers. *Annals of Epidemiology* 5:407-12.

122. Wolfe, W.H., J.E. Michalek, J.C. Miner, A. Rahe, J. Silva, W.F. Thomas, W.D. Grubbs, M.B. Lustik, T.G. Karrison, R.H. Roegner, and D.E. Williams. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. I. Physical health. *Journal of the American Medical Association* 264:1824-31.

123. Zafar, M.B., and M.K. Terris. 2001. Prostate cancer detection in veterans with a history of Agent Orange exposure. *The Journal of Urology* 166:100-3.

124. U.S. Centers for Disease Control. 1990. The association of selected cancers with service in the U.S. military in Vietnam. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, Center for Environmental Health and Injury Control, Agent Orange Projects: Atlanta, GA.

125. Grubbs, W.D., W.H. Wolfe, J.E. Michalek, D.E. Williams, M.B. Lustik, A.S. Brockman, S.C. Henderson, F.R. Burnett, R.G. Land, D.J. Osborne, V.K. Rocconi, M.E. Schreiber, J.C. Miner, G.L. Henriksen, and J.A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1992 followup examination results. NTIS: AD A 304 306, 304 308-316. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

126. Visintainer, P.F., M. Barone, H. McGee, and E.L. Peterson. 1995. Proportionate mortality study of Vietnam-era veterans of Michigan. *Journal of Occupational and Environmental Medicine* 37:423-8.

127. Jarone, R.E., H.M. Hayes, R.N. Hoover, J.F. Rosenthal, L.M. Brown, L.M. Pottern, N. Javadpour, K.J. O'Connell, and R.E. Stutzman. 1991. Service in Vietnam and risk of testicular cancer. *Journal of the National Cancer Institute* 83:1497-9.

128. Michalek, J.E., B.R. Burnham, H.E. Marden, Jr., J.N. Robinson, V.V. Elequin, J.C. Miner, R.W. Ogershok, W.K. Sneddon, W.D. Grubbs, B.C. Cooper, R.G. Land, V.K. Rocconi, M.E. Yeager, D.E. Williams, and M.E.B. Owens. 2000. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1997 follow-up examination results. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

129. Axelson, O. 1993. Seveso: Disentangling the dioxin enigma? *Epidemiology* 4:389-92.

130. Bailar, J.C., 3rd. 1991. How dangerous is dioxin? *New England Journal of Medicine* 324:260-2.

131. Collins, J.J., J.F. Acquavella, and B.R. Friedlander. 1992. Reconciling old and new findings on dioxin. *Epidemiology* 3:65-9.

132. Collins, J.J. 1993. Misclassified sarcomas and confounded dioxin exposure. *Epidemiology* 4:187-8.

133. Constable, J.D., R. Timperi, R. Clapp, K. Antman, and B. Boynton. 1987. Vietnam veterans and soft tissue sarcoma. *Journal of Occupational Medicine* 29:726.

134. Fingerhut, M.A., K. Steenland, M.H. Sweeney, W.E. Halperin, L.A. Piacitelli, and D.A. Marlow. 1992. Old and new reflections on dioxin. *Epidemiology* 3:69-72.

135. Hardell, L. 1994. TCDD carcinogenicity in humans. *Environmental Health Perspectives* 102: 814-5.

136. Hardell, L., and M. Eriksson. 1991. The association between cancer mortality and dioxin exposure: a comment on the hazard of repetition of epidemiological misinterpretation. *American Journal of Industrial Medicine* 19:547-9.

137. Kayajanian, G. 1997. Dioxin is a promoter blocker, a promoter, and a net anticarcinogen. *Regulatory Toxicology and Pharmacology* 26:134-7.

138. Kayajanian, G.M. 1999. Dioxin is a systemic promoter blocker, II. *Ecotoxicology and Environmental Safety* 42:103-9.

139. Kayajanian, G.M. 2000. Southeast Asia, promotability and dioxin's relationship to cancer incidence in Operation Ranch Hand veterans. *Ecotoxicology and Environmental Safety* 46:125-9.

140. Kayajanian, G.M. 2000. Arsenic, dioxin, and the promotional step in cancer creation. *Ecotoxicology and Environmental Safety* 45:195-7.

141. Kayajanian, G.M. 2001. Dioxin body burdens in operation ranch hand veterans: Promotion blocking and cancer causation. *Ecotoxicology and Environmental Safety* 50:167-73.

142. Kayajanian, G.M. 2002. The J-shaped dioxin dose response curve. *Ecotoxicology and Environmental Safety* 51:1-4.

143. Levallois, P., and P. Ayotte. 1995. Cancer incidence and dioxin exposure. *Epidemiology* 6:197-8.

144. Merlo, F., and R. Puntoni. 1986. Soft-tissue sarcomas, malignant lymphomas, and 2,3,7,8-TCDD exposure in Seveso. *Lancet* 2:1455.

145. Mundt, K.A., and L.D. Dell. 1998. Re: Cancer mortality in workers exposed to phenoxy herbicides, chlorophenols, and dioxins. An expanded and updated international cohort study. *American Journal of Epidemiology* 147:1094-5.

146. Puntoni, R., F. Merlo, A. Fini, L. Meazza, and L. Santi. 1986. Soft tissue sarcomas in Seveso. *Lancet* 2:525.

147. Rodricks, J.V., J.J. Collins, W.H. Farland, and D.J. Tollerud. 2001. Contrasting roles of epidemiology in dioxin-related policy: Lessons learned. *American Journal of Epidemiology* 154:S43-9.

148. Sinks, T. 1993. Misclassified sarcomas and confounded dioxin exposure. *Epidemiology* 4:3-6.

149. Smith, A.H., and P. Lopipero. 2001. Invited commentary: How do the Seveso findings affect conclusions concerning TCDD as a human carcinogen? *American Journal of Epidemiology* 153:1045-7.

150. Steele, E.J., A.J. Bellett, P.J. McCullagh, and B. Selinger. 1990. Reappraisal of the findings on Agent Orange by the Australian Royal Commission. *Toxicology Letters* 51:261-8.

151. Sternberg, S.S. 1994. Is dioxin a human carcinogen? *Science* 263:1545-6.

152. Stone, R. 1993. New Seveso findings point to cancer. *Science* 261:1383.

153. Swaen, G.M. 1997. Re: "Exposure to polychlorinated dioxins and furans (PCDD/F) and mortality in a cohort of workers from a herbicide-producing plant in Hamburg, Federal Republic of Germany." *American Journal of Epidemiology* 146:361-3.

154. Young, A.L., and G.M. Reggiani. 1991. Re: letter to the editor on "Agent Orange and its associated dioxins: Assessment of a controversy." *American Journal of Industrial Medicine* 19:399-405.

155. Zahm, S.H. 1995. Epidemiologic research on Vietnam veterans. Difficulties and lessons learned. *Annals of Epidemiology* 5:414-6.

156. Ayres, S.M., K.B. Webb, R.G. Evans, and J. Mikes. 1985. Is 2,3,7,8-TCDD (dioxin) a carcinogen for humans? *Environmental Health Perspectives* 62:329-35.

157. Becher, H., and D. Flesch-Janys. 1998. Dioxins and furans: Epidemiologic assessment of cancer risks and other human health effects. *Environmental Health Perspectives* 106(Suppl 2):623-4.

158. Boroush, M., and M. Gough. 1994. Can cohort studies detect any human cancer excess that may result from exposure to dioxin? Maybe. *Regulatory Toxicology and Pharmacology* 20:198-210.

159. Crump, K.S., R. Canady, and M. Kogevinas. 2003. Meta-analysis of dioxin cancer dose response for three occupational cohorts. *Environmental Health Perspectives* 111:681-7.

160. Hall, W. 1989. The logic of a controversy: The case of Agent Orange in Australia. *Social Science and Medicine* 29:537-44.

161. Hiremath, C., D. Bayliss, and S. Bayard. 1986. Qualitative and quantitative cancer risk assessment. *Chemosphere* 15:1815-23.

162. Kogevinas, M. 2001. Human health effects of dioxins: Cancer, reproductive and endocrine system effects. *Human Reproduction Update* 7:331-9.

163. Lilienfeld, D.E., and M.A. Gallo. 1989. 2,4-D, 2,4,5-T, and 2,3,7,8-TCDD: An overview. *Epidemiologic Reviews* 11:28-58.

164. Scheuplein, R.J., and J.C. Bowers. 1995. Dioxin—an analysis of the major human studies: Comparison with animal-based cancer risks. *Risk Analysis* 15:319-33.

165. Smith, A.H., and M.L. Warner. 1992. Biologically measured human exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin and human cancer. *Chemosphere* 25:219-22.

166. Starr, T.B. 2001. Significant shortcomings of the U.S. Environmental Protection Agency's latest draft risk characterization for dioxin-like compounds. *Toxicological Sciences* 64:7-13.

167. Tollefson, L. 1991. Use of epidemiology data to assess the cancer risk of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Regulatory Toxicology and Pharmacology* 13:150-69.

168. Johnson, E.S. 1991. Human exposure to 2,3,7,8-TCDD and risk of cancer. *Critical Reviews in Toxicology* 21:451-63.

169. Watanabe, S., K. Kitamura, and M. Nagahashi. 1999. Effects of dioxins on human health: A review. *Journal of Epidemiology/Japan Epidemiological Association* 9:1-13.

170. Zober, A., P. Messerer, and M.G. Ott. 1997. BASF studies: Epidemiological and clinical investigations on dioxin-exposed chemical workers. *Teratogenesis, Carcinogenesis, and Mutagenesis* 17:249-56.

171. Crump, K.S., R. Canady, and M. Kogevinas. 2003. Meta-analysis of dioxin cancer dose response for three occupational cohorts. *Environmental Health Perspectives* 111:681-87.

172. T.B. Starr. 2003. Significant issues raised by meta-analysis of cancer mortality and dioxin exposure. *Environmental Health Perspectives* 111:1443-7.

173. Mackie, D., J. Liu, Y.S. Loh, and V. Thomas. 2003. No evidence of dioxin cancer threshold. *Environmental Health Perspectives* 111:1145-7.

174. Aylward, L., C. Kirman, D. Cher, and S. Hays. 2003. Re: Analysis of dioxin cancer threshold. *Environmental Health Perspectives* 111:A510.

175. Birnbaum, L.S., and S.E. Fenton. 2003. Cancer and developmental exposure to endocrine disruptors. *Environmental Health Perspectives* 111:389-94.

176. Frumkin, H. 2003. Agent Orange and cancer: An overview for clinicians. *Ca: A Cancer Journal for Clinicians* 53:245-55.

177. Cole, P., D. Trichopoulos, H. Pastides, T. Starr, and J.S. Mandel. 2003. Dioxin and cancer: A critical review. *Regulatory Toxicology and Pharmacology* 38:378-88.

178. Thomas, W.F., W.D. Grubbs, T.G. Karrison, M.B. Lustik, R.H. Roegner, D.E. Williams, W.H. Wolfe, J.E. Michalek, J.C. Miner, and R.W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

179. Akhtar F., D.H. Garabrant, N.S. Ketchum, and J.E. Michalek. 2004. Cancer in US Air Force veterans of the Vietnam War. *Journal of Occupational and Environmental Medicine* 46(2):123-36.

180. Institute of Medicine. 1994. Health Effects of Herbicides used in Vietnam. National Academy Press: Washington, DC.

181. Institute of Medicine. 1997. Veterans and Agent Orange: Update 1996. National Academy Press: Washington, DC.

182. Institute of Medicine. 1999. Veterans and Agent Orange: Update 1998. National Academy Press: Washington, DC.

183. Institute of Medicine. 2001. Veterans and Agent Orange: Update 2000. National Academy Press: Washington DC.

184. Garrow, J.S., and J. Webster. 1985. Quetelet's index (W/H^2) as a measure of fatness. *International Journal of Obesity* 9:147-53.

185. Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L. R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

186. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57:369-78.

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11 NEUROLOGY ASSESSMENT

11.1 INTRODUCTION

11.1.1 Background

11.1.1.1 Organs/Diseases

The Air Force Health Study (AFHS) neurology assessment included the evaluation of cranial nerve function, peripheral nerve status, and central nervous system (CNS) coordination processes based on a physical examination. The cranial nerve function incorporated smell, visual fields, light reaction, ocular movement, facial sensation, corneal reflex, jaw clench, smile, palpebral fissure, balance, gag reflex, speech, tongue position relative to midline, palate and uvula movement, and shoulder shrug. Peripheral nerve status was assessed by light pinprick, light touch (with cotton sticks), visual inspection of muscle mass (and palpation, if indicated), three deep tendon reflexes (patellar, Achilles, and biceps), and the Babinski reflex. In addition, indices of bilateral symmetric distal sensory or sensorimotor polyneuropathy were analyzed based on testing of ankle and toe flexor strength, equilibrium (Romberg sign), Achilles reflex, light touch, pinprick, vibration at the ankle, and joint position of the left and right great toes. The evaluation of CNS coordination processes was based on tremor, coordination, Romberg sign, and gait. Neurobehavioral endpoints, which have been the subject of intensive investigation in this and other studies of Vietnam veterans, are considered separately in Chapter 12, Psychology Assessment.

11.1.1.2 Toxicology

The mechanism by which dioxin could result in neurotoxic effects is not well-known (1), although it has been suggested that the aryl hydrocarbon (Ah) receptor plays a role in neurotoxicity (2). Several studies have investigated the neurotoxic effects of dioxin in laboratory animals with inconsistent results. Rats given a high dose of dioxin (1,000 µg/kg) intraperitoneally demonstrated no apparent neurological deficits (3). The intracerebroventricular administration of dioxin proved far more toxic than the subcutaneous route in producing a wasting syndrome in rats, although specific neurological indices were not examined (4). In another study, the neuromuscular effects associated with acute lethal doses of dioxin in rats were primarily in muscle tissue rather than peripheral nerves (5). A study of Wistar rats receiving a single intraperitoneal low dose of dioxin in one of four strengths documented dose-dependent and statistically significant reductions in motor and sensory nerve conduction velocities relative to the controls (6). Ten months after exposure, microscopic studies confirmed the histologic appearance of a severe peripheral neuropathy of the axonal and demyelinating type (7). No other studies in animals, however, found a similar effect (1).

11.1.1.3 Epidemiology

In humans, only circumstantial evidence linking 2,4-D herbicide exposure to neurotoxicity exists; the arguments against a causal relation were summarized by Mattsson and Eisenbrandt (8). Nevertheless, a host of neurological symptoms have been reported following dioxin exposure. These symptoms were grouped under the generic term "neurasthenia." Numerous studies were published describing neurological sequelae in populations exposed to dioxin by occupation (9-16), environmental contamination (17-21) and industrial accidents (22-28), and in association with service in Southeast Asia

(SEA) during the Vietnam War (29-36). Epidemiologic studies of neurological sequelae of dioxin exposure were reviewed recently (37) and are discussed in some detail below.

The potential health effects of environmental exposure to dioxin due to industrial accidents were examined in several epidemiologic studies. The 1976 chemical explosion in Seveso, Italy, provided a basis for numerous reports on the exposed population (22-25, 27, 28). Several of these reports included clinical and laboratory indices in the examination protocols, most of which focused on signs and symptoms of peripheral neuropathy as primary clinical endpoints. In one study, 152 subjects with chloracne, a marker for high-level dioxin exposure, were compared with 123 age- and sex-matched controls from nearby towns. Only 1 of 13 neurophysiologic indices (i.e., sensory nerve action potential) was found to be statistically significantly different (p<0.02) between exposed and unexposed subjects, and none of the exposed subjects was found to have a peripheral neuropathy according to World Health Organization criteria (25). Investigators of the Seveso population who included electromyographic studies in the examination protocols reached similar conclusions (22, 24, 27), as did those studying the populations exposed following uncontrolled chemical reactions that occurred in Germany in 1953 (26) and in Nitro, West Virginia, in 1949 (12).

Point-source environmental exposure to dioxin also has been the focus of numerous epidemiologic studies, some of which included neurological indices in their protocols (17-21). In 1971, waste byproducts contaminated with dioxin were mixed with oils and widely sprayed for dust control in residential areas in eastern Missouri. Soil concentrations in some areas reached 2,200 parts per billion, far exceeding the highest degree of ground contamination that occurred at Seveso (21). Comprehensive medical evaluations of exposed and unexposed cohorts included detailed neurological examinations (17-20) and, in one report (19), quantitative studies of tactile, vibratory, and thermal sensory perception. None of the Missouri dioxin studies (21) revealed any clinical evidence for central or peripheral neurological disease associated with exposure to dioxin. In one Missouri study that related neurological endpoints to tissue levels of dioxin (18), no associations were found among 41 subjects between the body burden of dioxin and abnormalities in deep tendon reflexes or pain and vibratory sensation.

Some occupational studies investigated the potential neurological effects of dioxin exposure, such as motor or coordination dysfunction (9, 15, 26). An epidemiologic study conducted by the National Institute of Occupational Safety and Health is one of a few that relates serum dioxin levels to neurological indices (15). The prevalence of peripheral neuropathy was determined in 265 workers with a mean serum dioxin level of 220 parts per trillion (ppt) 15 years after exposure and in 244 referents with a level of 7 ppt. The diagnosis of peripheral neuropathy was established by symptoms and by data collected during physical examination, electrophysiologic studies, and quantitative sensory testing. There was no evidence of a long-term effect of dioxin exposure on peripheral neuropathy.

Other occupational studies evaluating neurological symptoms revealed inconsistent results. In a study of 109 workers employed in a Chinese chemical manufacturing plant, nerve conduction velocities were observed to be slower among workers in an area where exposure to dioxin was highest (16). On the other hand, findings from a morbidity follow-up study of 158 men exposed to dioxin after a chemical accident at the trichlorophenol unit of a BASF chemical facility were inconclusive (26). Exposure to dioxin was determined based on chloracne status and extrapolated blood lipid concentrations. The rate of episodes of illness among exposed workers was compared to the rate in an unexposed population employed at the same facility. Although more frequent episodes of a variety of nervous system disorders may have been related to high dioxin exposure, no evidence for specific peripheral nervous system disorders, such as peripheral neuropathy, was observed.

One occupational study of 47 railroad workers examined 6 years after exposure to polychlorinated phenols (including dioxin) during the cleanup of a chemical spill revealed evidence, through electrophysiologic measurements, of a peripheral neuropathy in 43 of these workers. High prevalence of dystonia (53%) and tremor (78%) were documented (9). In another study, neuralgia was found in 30 percent of 159 workers exposed to chemicals in a herbicide production plant (38). In a recent study of 13 workers involved in herbicide production in the Czech Republic, clinical polyneuropathic signs were found in 38 percent of the employees (39). In addition, electroencephalography abnormalities were found more frequently in workers exposed to higher levels of the herbicide, based on blood dioxin levels (39). The findings in these studies, however, were not contrasted with those in the unexposed control population.

The relation between pesticide exposure and Parkinson's disease was evaluated in 1996, 1998, 2000, and 2002 Institute of Medicine (IOM) reports (1, 40-42). Some indication of an association was seen based on a review of 30 epidemiologic studies, most of which were case-control studies focusing on occupational exposure. An association of Parkinson's disease with exposure to dioxin, however, was not reported in any of these studies. Therefore, the 2002 IOM committee considered the evidence for an association of Parkinson's disease with exposure to dioxin to be inadequate or insufficient (1). A similar conclusion was reached for amyotrophic lateral sclerosis based on a review of five epidemiologic studies, none of which evaluated dioxin exposure specifically (1).

Few studies of Vietnam veterans have incorporated neurological data into their protocols and, with the exception of the AFHS (31-34, 43), none has correlated neurological indices with tissue levels of dioxin. One large-scale study of American Legion veterans who served in Vietnam found an increased incidence of reported neurobehavioral disorders among veterans who reported exposure to herbicides (29).

The Vietnam Experience Study, conducted by the Centers for Disease Control and Prevention (CDC), compared the health status of 2,490 Vietnam veterans with 1,972 non-Vietnam veterans (30). The study protocol included comprehensive neurological examinations, nerve conduction velocity studies, and neurophysiologic indices of vibratory, thermal, and auditory sensations. Aside from an increased prevalence of combat-related high frequency hearing loss in a pattern consistent with prior noise exposure, no neurological abnormalities were noted in association with service in Vietnam. A recent study found no increased prevalence of neurological symptoms across levels of exposure to Agent Orange among 1,224 Korean Vietnam veterans, although the risk of peripheral neuropathy was higher among veterans than nonveterans (36).

The evidence for an association between serum dioxin levels and peripheral neuropathy among Ranch Hand personnel in the AFHS was recently reviewed for the examination years 1982, 1985, 1987, 1992, and 1997 (43). Each Ranch Hand veteran was assigned to one of three dioxin categories (background, low, or high) based on his serum dioxin level. In addition, an unexposed comparison group was selected comprising Air Force veterans who served in SEA during the same time period as the Ranch Hand veterans, but who were not involved with spraying herbicides. Neurological parameters evaluated at the physical examinations included nerve conduction velocity (1982), vibrotactile threshold (1992 and 1997), and symmetrical peripheral abnormalities (all examination years). Peripheral neuropathy was classified as possible, probable, or definite based on the number of signs of peripheral abnormality. No evidence pointed to an association between serum dioxin levels and nerve conduction velocity. Relative risk estimates for any symmetrical peripheral abnormality or possible symmetrical peripheral neuropathy varied little across categories of serum dioxin, with most odds ratios around unity. Only in the 1997 examination was there some indication of an increased risk for these outcomes reported in the highest exposure level (odds ratio=1.8; 95% confidence interval: 1.2-2.7). Some indication for an association with probable peripheral neuropathy was found in the years 1985, 1992, and 1997. Although dose-

response patterns were somewhat inconsistent, in these years the highest risk was observed in the highest exposure group. Finally, in 1992 and 1997, the risk of diagnosed peripheral neuropathy, but not vibrotactile abnormality, was associated with dioxin levels.

In a 1996 report published by the IOM (42), the committee concluded that there is "limited/suggestive" evidence of an association between exposure to certain herbicides used in Vietnam and the development of an acute or subacute transient peripheral neuropathy. This conclusion remained unaltered in the 2002 IOM report (1). The evidence regarding the association between exposure to dioxin and disorders involving persistent peripheral neuropathy, or motor or coordination deficits, was considered inadequate or insufficient (1).

11.1.2 Summary of Previous Analyses of the Air Force Health Study

11.1.2.1 1982 Baseline Examination Summary Results

The 1982 AFHS neurology assessment consisted of questionnaire, physical examination, and electromyographic data obtained by examiners and technicians who were blind to the group identity of each participant. The physical examination required an average of 30 minutes to complete. Analyses were adjusted for reported alcohol usage, exposure to insecticides and industrial chemicals, and glucose intolerance (diabetes).

Results of the questionnaire disclosed no significant group differences in reported neurological diseases. The physical examination did not reveal any statistically significant group differences in the function of the 12 cranial nerves. Peripheral nerve function was assessed by the quality of four reflexes (patellar, Achilles, biceps, and Babinski); muscle strength or bulk; and reaction to the stimuli of pinprick, light touch, and vibration. Other than a statistically significant increase (p=0.03) in abnormal Babinski reflexes among Ranch Hands, significant group differences were not detected.

Nerve conduction velocities were obtained on the ulnar nerve above and below the elbow and the peroneal nerve. The results for each segmental measurement were nearly identical in the Ranch Hand and Comparison groups. Conduction velocity showed highly significant inverse relations to both alcohol use and diabetes in almost all of the anatomic measurements. No group associations or interactions were detected with the reported exposure to industrial and degreasing chemicals and insecticides.

No significant group differences were detected in four measures of central neurological function (tremor, finger-nose coordination, modified positive Romberg sign, or abnormal gait). Alcohol usage was significantly associated with the presence of tremor, and glucose intolerance was highly correlated to abnormal balance and the presence of tremor.

11.1.2.2 1985 Follow-up Examination Summary Results

The 1985 AFHS neurological examination did not include the measurements of nerve conduction velocities, but otherwise repeated the baseline examination protocol. The questionnaire maintained a historical focus on neurasthenia through five questions for the 1982–1985 interval. With this similarity in examination and questionnaire, the dependent variables of the analyses were the same as those of the baseline study.

Interval questionnaire data (1982–1985) on neurological illness, verified by medical records, revealed no significant group differences. These data were added to verified baseline examination historical

information to assess possible differences in the lifetime experience of neurological disease. Again, there was no significant difference between the Ranch Hand and Comparison groups.

The neurological examination evaluated neurological integrity in three broad areas: cranial nerve function, peripheral nerve status, and CNS coordination. Assessment of the 12 cranial nerves was based on the measurement of 15 variables. Two summary indices were constructed, and no statistically significant differences between groups were found. In contrast to the baseline examination, there was no significant group difference in Babinski reflex. The analyses of peripheral nerve function, as measured by eight variables (four reflexes, three sensory determinations, and muscle mass), did not reveal significant group differences. Coordination was evaluated by four measurements and a constructed summary variable. The CNS summary index showed significant adverse effects for Ranch Hands.

In conclusion, none of the 27 neurological variables demonstrated a significant group difference, although several showed an aggregation of abnormalities in the Ranch Hand group, which emphasized the need for continued surveillance. Historical reporting of neurological disease was similar in both groups. The longitudinal analyses disclosed a reversal of significant increase among Ranch Hands in Babinski reflex abnormalities at the baseline examination to a nonsignificant difference between groups (RR=1.02) at the 1985 follow-up examination.

11.1.2.3 1987 Follow-up Examination Summary Results

The neurological health of the Ranch Hand group was not substantially different from the Comparison group. For the questionnaire variables related to neurological disease, Ranch Hands had significantly more hereditary and degenerative diseases, such as benign essential tremor. The statistical results of the group contrasts for 30 physical examination variables relating to cranial nerve function, peripheral nerve status, and CNS coordination processes generally were not significant, except for the analysis of coordination. Significantly more coordination abnormalities were found in Ranch Hands than Comparisons. The longitudinal analyses for the cranial nerve index and the CNS index revealed no significant differences.

11.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Examination Summary Results

Overall, the neurology assessment did not indicate that dioxin was associated with neurological disease, although some analyses revealed a significant association between dioxin levels and CNS index and coordination. The adjusted analyses for the historical questionnaire variables were not significant and few statistically significant results were noted for the physical examination variables. The group contrast from the 1987 follow-up examination found that Ranch Hands had significantly more hereditary and degenerative diseases (mostly benign essential tremor) than Comparisons, but the serum dioxin analyses provided no support for the hypothesis that dioxin levels were associated with an increased risk of these diseases. The adjusted categorized dioxin analyses found that Ranch Hands in the high dioxin category had more coordination abnormalities than Comparisons. This was consistent with the previous analysis of the 1987 follow-up examination data, where the Ranch Hand group had significantly more coordination abnormalities than the Comparison group (1.5 percent versus 0.6 percent). The serum dioxin analyses showed significant adverse associations with the CNS index in the initial dioxin, 1987 dioxin, and categorized dioxin analyses.

11.1.2.5 1992 Follow-up Examination Summary Results

Overall, the neurology assessment found the prevalence of neurological disease to be comparable between the Ranch Hand and Comparison groups, and showed no consistent evidence of a dose-response effect

with either estimated initial dioxin levels or 1987 dioxin levels. In the group contrasts stratified by occupation, Ranch Hand enlisted groundcrew had significantly more cranial nerve index abnormalities than Comparison enlisted groundcrew. The enlisted groundcrew was the military occupation category with the highest median level of dioxin; however, analyses of serum dioxin levels did not exhibit a dose-response trend.

11.1.2.6 1997 Follow-up Examination Summary Results

Four neurological disorders and extensive physical examination data on cranial nerve function, peripheral nerve status, and CNS coordination processes were analyzed in the neurology assessment. Inflammatory diseases verified by a medical records review found a significant excess among Ranch Hands (n=7) relative to Comparisons (n=1); however, three of the seven Ranch Hand diseases were caused by bacterial infections, suggesting that this finding was unrelated to herbicide or dioxin exposure. Peripheral disorders, as verified by a medical records review, increased in Ranch Hands as levels of 1987 dioxin increased. Neck range of motion abnormalities were increased in Ranch Hands relative to Comparisons in terms of both a group designation and categorized dioxin levels. The increase in abnormalities for Ranch Hands relative to Comparisons was noted in enlisted flyers. An increase in the risk of an abnormal muscle status was observed in Ranch Hand enlisted groundcrew. A significant association between initial dioxin and both visual field and patellar reflex abnormalities was observed. Indices of polyneuropathy showed an increase in the prevalence of abnormality in Ranch Hands relative to Comparisons and a significant positive association with initial and 1987 dioxin levels. The clinical importance of the increased risk of polyneuropathy was uncertain due to the small number of affected veterans.

In summary, although a common etiology in these findings was not apparent, a statistically significant increase in neurological disease appeared in Ranch Hands historically, on physical examination, and as reflected in several of the composite polyneuropathy indices. Further, the significant associations of neck range of motion abnormalities with categorized dioxin and a history of peripheral disorders with 1987 dioxin levels provided evidence of an association of neurological disease with elevated dioxin levels. The results of the analysis of the polyneuropathy indices also provided support of an association between elevated dioxin levels and neurological disease; however, the clinical importance of this finding was uncertain.

11.1.3 Parameters for the 2002 Neurology Assessment

11.1.3.1 Dependent Variables

The neurology assessment was based on extensive physical examination data on cranial nerve function, peripheral nerve status, and CNS coordination processes. This information was supplemented by verified histories of neurological diseases. Participants who tested positive for syphilis and participants who tested positive for the human immunodeficiency virus (HIV) were excluded from the analysis of all dependent variables. Hamilton AT® equipment was used for automated dilution of specimens for HIV testing, and the amount of virus antibody present in the serum was produced and measured using a spectrophotometer. Presence or absence of syphilis was determined through a venereal disease research laboratory (VDRL) test using Difco® agglutination assays. The positive VDRL tests were confirmed using the fluorescent treponemal antibody absorption (FTA-ABS) test.

11.1.3.1.1 Medical Records Variables

The 2002 questionnaire captured data on the occurrence of neurological disorders. Medical records review was accomplished to confirm reported neurological disorders and to identify any unreported

neurological conditions for each participant that attended the 2002 physical examination. These data from the 2002 physical examination were combined with data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations to form a complete history of neurological disorders for each participant. Neurological diseases and disorders were classified into four categories of the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) manual: inflammatory diseases (ICD-9-CM codes 320.0–326), hereditary and degenerative diseases (ICD-9-CM codes 330.0–337.9), peripheral disorders (ICD-9-CM codes 350.1-359.9), and other neurological disorders (ICD-9-CM codes 340–349.9). The majority of other neurological disorders were unspecified encephalopathies, but conditions such as multiple sclerosis, other demyelinating diseases of the CNS, hemiplegia, other paralytic syndromes, epilepsy, migraine, catalepsy or narcolepsy, other conditions of the brain, and other unspecified disorders of the CNS were included. Each of the four categories of disorders was coded as "yes" or "no." The analyses performed in this chapter were based on the 1,951 participants who attended the 2002 follow-up examination.

Participants with a verified pre-SEA history of the disorder under study were excluded from all analyses pertaining to that disorder.

11.1.3.1.2 Physical Examination Variables

The physical examination included various indicators of cranial nerve function, peripheral nerve status, and CNS coordination processes.

11.1.3.1.2.1 Cranial Nerve Function

The evaluation of cranial nerve function was based on the following 15 variables: smell, visual fields, light reaction, ocular movement, facial sensation, corneal reflex, jaw clench, smile, palpebral fissure, balance, gag reflex, speech, tongue position relative to midline, palate and uvula movement, and shoulder shrug. All of these variables were scored as "normal" or "abnormal," except for jaw clench and palate and uvula movement, which were scored as "symmetric" or "deviated." For variables with left and right determinations, the two results were combined to produce a single normal or abnormal result, where normal indicated that both responses were normal, and abnormal indicated that at least one of the responses was abnormal. Abnormal speech conditions included aphasia, dysarthria, agnosia, and other speech abnormalities.

A cranial nerve index was created by combining responses for the 15 cranial nerve parameters. This index was classified as abnormal if at least one of the determinations was abnormal, and was classified as normal if all of the cranial nerve parameters were normal.

11.1.3.1.2.2 Peripheral Nerve Status

Peripheral nerve status was assessed by light pinprick, light touch (cotton sticks), visual inspection of muscle mass (and palpation, if indicated), three deep tendon reflexes (patellar, Achilles, and biceps), and the Babinski reflex. In addition, three indices to assess bilateral symmetric distal sensory or sensorimotor polyneuropathy were analyzed. These indices were constructed based on testing of ankle and toe flexor strength, equilibrium (Romberg sign), Achilles reflexes, light touch, pinprick, vibration at the ankle, and joint position of the left and right great toes.

Pinprick and light touch were considered normal if the reaction was normal on both legs. A variable to judge muscle status was constructed using data on bulk; tone of upper and lower extremities; and the strength of distal wrist extensors, ankle and toe flexors, proximal deltoids, and hip flexors. Bulk was

classified as either "normal" or "abnormal." Tone was classified as "abnormal" if there was either a decreased or increased response on either the left side, right side, or both sides. The strength of distal wrist extensors, ankle and toe flexors, proximal deltoids, and hip flexors was considered "abnormal" if either the left or right side or both sides were decreased. Composite muscle status was classified as "normal" if all of the components were normal on both the left and right sides and "abnormal" if at least one of the components was abnormal on either or both sides.

The patellar, Achilles, and biceps reflexes were divided into three categories: "absent," "sluggish," and "active or very active." The categories of "active" and "very active" were combined because of the sparse number of participants with very active reflexes. Two contrasts that preserved the ordinal structure of the data were examined: "sluggish or absent" versus "active or very active" (i.e., less than active versus active), and "absent" versus "sluggish, active, or very active" (i.e., reflexes absent versus not absent). When the assessments of the reflex were different between the left and right body side, the more severe condition was assigned. For example, if the left Achilles reflex was sluggish and the right Achilles reflex was absent, the composite Achilles reflex variable was designated as absent.

Three indices were used to assess bilateral peripheral neuropathy. The endpoints discussed previously in this section assessed unilateral abnormalities, whereas these indices assessed bilateral abnormalities and were considered abnormal only if both the left and right determinations were abnormal. These indices were based on the following seven conditions or sets of conditions:

1. Both left and right ankle and toe flexors were abnormal (no, yes)

2. The Romberg sign (equilibratory) was abnormal (no, yes)

3. Both left and right Achilles reflexes were absent (no, yes)

4. Reaction to a light touch was abnormal on both the left and right legs (no, yes)

5. Reaction to a pinprick was abnormal on both the left and right legs (no, yes)

6. Both left and right ankle vibrations (128 Hz) were abnormal (no, yes)

7. The position of both the left and right great toe was abnormal (no, yes).

A symmetric peripheral abnormality index was coded as "present" if the response to any of the above seven bilateral conditions listed above was "yes." A second index, termed a possible peripheral neuropathy indicator, was coded as "abnormal" if at least one of the following three conditions was found bilaterally: (1) absent Achilles reflex, (2) abnormal vibration at the ankle, or (3) abnormal pinprick (feet). If two of the three above conditions were present bilaterally, a third index, termed probable peripheral neuropathy index, was coded as "present"; otherwise, the probable peripheral neuropathy index was coded as "absent."

Participants with peripheral edema in the lower extremities were excluded from the analyses of pinprick and light touch. The analysis of the Achilles reflex and the patellar reflex excluded participants with a transient or sustained clonus in these reflexes, respectively. Participants with quadriplegia (ICD-9-CM codes 344.00-344.09), paraplegia (ICD-9-CM code 344.1), injuries (ICD-9-CM codes 806.0-806.9, 907.2-907.9, and 952.0-957.9), amputations (ICD-9-CM codes 887.0-887.7, 897.0-897.7, and procedure codes X84.00-X84.19), or alcohol-related disorders (ICD-9-CM 291.0-291.9, 303.00-303.93, 305.00-305.03, 357.5, 425.5, and 571.0-571.3) were excluded from the symmetric, possible, and probable peripheral neuropathy indicators. As with the other dependent variables in this section, participants who tested positive for syphilis and participants who tested positive for HIV were excluded for all peripheral nerve status dependent variables.

11.1.3.1.2.3 CNS Coordination Processes

The evaluation of CNS coordination processes was based on the analyses of the following variables: tremor, coordination, Romberg sign, gait, and a CNS index. For these variables, multiple determinations, which included left and right as well as upper and lower responses, were combined to form a single result. A result was classified as "normal" if all determinations were normal and "abnormal" if at least one determination was abnormal. Tremor was examined for the left and right upper and lower extremities. Abnormal tremors included resting, essential, intention, and "other tremors." Coordination was a composite index defined as "normal" if the Romberg sign, finger-nose-finger and heel-knee-shin coordination processes, rapidly alternating movements of pronation and supination of hands, and rapid patting were normal. The Romberg sign variable was equivalent to the "balance" variable analyzed as part of the cranial nerve function assessment. The gait variable was based on the examining physician's assessment of the participant's gait. An abnormal gait included conditions such as broad-based, small-stepped, ataxic, or other irregular gait patterns. A CNS index was constructed and based on a composite variable of tremor, coordination, and gait. This index was coded as "normal" if all three of the components were normal and "abnormal" if otherwise.

11.1.3.2 Covariates

Age, race, military occupation, body mass index, lifetime alcohol history, cumulative exposure to insecticides or pesticides, cumulative exposure to industrial chemicals, cumulative exposure to degreasing chemicals, diabetic class, and duration of diabetes were covariates for all adjusted statistical analyses. The peripheral abnormality and neuropathy indicators (symmetrical, possible, and probable) were adjusted for reported exposure to heavy metals and vibrating power equipment in addition to the covariates listed above.

Age, race, and military occupation were determined from military records. Body mass index was calculated as weight/(height)^2, where the weight was measured in kilograms and the height was measured in meters at the physical examination (44). For purposes of covariate associations for discrete dependent variables, body mass index was dichotomized as "not obese" ($\leq$30 kg/m^2) and "obese" (>30 kg/m^2).

Lifetime alcohol history was based on information from the 2002 questionnaire and combined with similar information gathered at the 1987, 1992, and 1997 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking pattern changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year. Current alcohol use was defined as the average number of drinks per day during the 2 weeks prior to completing the physical examination.

The participants' cumulative exposures through 1997 to insecticides or pesticides, industrial chemicals, and degreasing chemicals were updated with information, as reported by the participant, in the 2002 questionnaire.

In the 2002 questionnaire, a general screening question on diabetes was posed. During the in-person health interview each participant was asked: "Since the date of the last interview, has a doctor told you for the first time that you had diabetes?" Medical records review was accomplished to confirm reported diabetes and to identify any unreported diabetes for each participant that attended the 2002 physical examination. These data from the 2002 physical examination were combined with data from the 1982

baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations to form a complete history of diabetes for each participant. The analyses performed in this chapter were based on the 1,951 participants who attended the 2002 follow-up examination. Participants with a verified history of diabetes, as diagnosed previously by a physician, were combined with those participants with either

- a 2-hour postprandial glucose level of 200 mg/dL or greater on two separate occasions

- a fasting glucose level of 126 mg/dL or greater on two separate occasions, or

- one 2-hour postprandial glucose measurement ≥200 mg/dL and one fasting glucose ≥126 mg/dL on two separate occasions,

and classified as "diabetic" for the diabetic class covariate. Those participants not classified as "diabetic," as defined above, but with a 2-hour postprandial glucose level of at least 140 mg/dL or a fasting glucose level of at least 110 mg/dL at the 2002 physical examination, were classified as "impaired." Those participants not classified as "diabetic" or "impaired" as defined above were classified as "normal."

For each participant diagnosed as diabetic, a date of diagnosis was recorded. The difference between the date of diagnosis and the date of the 2002 physical examination was calculated to determine the duration of diabetes covariate. Participants who were newly diagnosed as diabetic at or after the 2002 physical examination were assigned a value of 0 years, as were nondiabetic participants.

Two additional covariates, exposure to heavy metals and exposure to vibrating power equipment or tools, were used for the peripheral abnormality or neuropathy indicator dependent variables. The 2002 questionnaire asked each study participant whether he had worked for 30 days or more with lead, mercury, chromium, nickel, copper, cadmium, manganese, arsenic, selenium, or molybdenum. Responses were combined to form a composite exposure to heavy metals covariate. Each participant also was asked in the 2002 questionnaire whether he had ever worked for 30 days or more with vibrating power equipment or tools. The response (yes or no) to this question also was used as a covariate in the assessment of the peripheral neuropathy indicator dependent variables.

11.1.4 Statistical Methods

Table 11-1 summarizes the statistical analysis performed for the 2002 neurology assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, exclusions, and statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 11-1.

Table 11-1. Statistical Analysis for the Neurology Assessment

Dependent Variables

Variable	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Inflammatory Diseases	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Hereditary and Degenerative Diseases	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Peripheral Disorders	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Other Neurological Disorders	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Smell	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Visual Fields	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Light Reaction	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Ocular Movement	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Facial Sensation	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Corneal Reflex	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Jaw Clench	PE	D	Deviated Symmetric	--	(b)	Descriptive
Smile	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Palpebral Fissure	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Balance	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Gag Reflex	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Speech	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Tongue Position Relative to Midline	PE	D	Deviated Symmetric	(1)	(b)	U:LR,CS A:LR
Palate and Uvula Movement	PE	D	Deviated Symmetric	--	(b)	Descriptive
Shoulder Shrug	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Cranial Nerve Index	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR

Variable	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Pinprick	PE	D	Abnormal Normal	(1)	(c)	U:LR,CS A:LR
Light Touch	PE	D	Abnormal Normal	(1)	(c)	U:LR,CS A:LR
Muscle Status	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Patellar Reflex	PE	D	Absent Sluggish Active or Very Active	(1)	(d)	U:PR,CS A:LR
Achilles Reflex	PE	D	Absent Sluggish Active or Very Active	(1)	(e)	U:PR,CS A:LR
Biceps Reflex	PE	D	Absent Sluggish Active or Very Active	(1)	(b)	U:PR,CS A:LR
Babinski Reflex	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Any Symmetrical Peripheral Abnormality	PE	D	Present Absent	(2)	(f)	U:LR,CS A:LR
Possible Peripheral Neuropathy	PE	D	Present Absent	(2)	(f)	U:LR,CS A:LR
Probable Peripheral Neuropathy	PE	D	Present Absent	(2)	(f)	U:LR,CS A:LR
Tremor	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Coordination	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Romberg Sign	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
Gait	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR
CNS Index	PE	D	Abnormal Normal	(1)	(b)	U:LR,CS A:LR

[a]Covariates:

(1) age, race, military occupation, lifetime alcohol history, body mass index, cumulative insecticide exposure, cumulative degreasing chemical exposure, cumulative industrial chemical exposure, diabetic class, duration of diabetes.

(2) age, race, military occupation, lifetime alcohol history, body mass index, cumulative insecticide exposure, cumulative degreasing chemical exposure, cumulative industrial chemical exposure, diabetic class, duration of diabetes, composite exposure to heavy metals, worked with vibrating power equipment or tools.

[b]Exclusions:

(a) participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with a verified pre-SEA history of the disorder.

(b) participants with positive serological tests for syphilis, participants who tested positive for HIV.

(c) participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with peripheral edema of the lower extremities.

(d) participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with unsustained or sustained clonus of the patellar reflex.

(e) participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with unsustained or sustained clonus of the Achilles reflex.

(f) participants with positive serological tests for syphilis, participants who tested positive for HIV, participants with quadriplegia, paraplegia, injuries, amputations, or alcohol-related disorders.

Covariates

Variable (units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	C/D	Born ≥ 1942 Born < 1942
Race	MIL	D	Black Non-Black
Military Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Lifetime Alcohol History (drink-years)	Q-SR	C/D	0 >0–40 >40
Body Mass Index (kg/m^2)	PE	C/D	Not Obese: ≤30 Obese: >30
Cumulative Insecticide Exposure	Q-SR	D	Yes No
Cumulative Degreasing Chemical Exposure	Q-SR	D	Yes No
Cumulative Industrial Chemical Exposure	Q-SR	D	Yes No
Diabetic Class	LAB/MR-V	D	• Diabetic: past history of diabetes, as diagnosed previously by a physician, or ≥200 mg/dL 2-hour postprandial glucose on two separate occasions, or ≥126 mg/dL fasting glucose on two separate occasions, or one 2-hour postprandial glucose ≥200 mg/dL and one fasting glucose ≥126 mg/dL on two separate occasions • Impaired: not diabetic; ≥140 mg/dL 2-hour postprandial glucose or ≥110 mg/dL fasting glucose • Normal: not diabetic or impaired; <140 mg/dL 2-hour postprandial glucose and <110 mg/dL fasting glucose
Duration of Diabetes (years)	LAB/MR-V	C/D	Nondiabetic or Newly Diagnosed Diabetic: 0 years Previously Diagnosed Diabetic: >0 years
Composite Exposure to Heavy Metals	Q-SR	D	Yes No
Worked With Vibrating Power Equipment or Tools	Q-SR	D	Yes No

Abbreviations

Data Source:	LAB: 2002 laboratory results
	MIL: Air Force military records
	MR-V: Medical records (verified)
	PE: 2002 physical examination
	Q-SR: AFHS health questionnaires (self-reported)
Data Form:	D: Discrete form of dependent variable or covariate
	C/D: Appropriate form for analysis (either continuous or discrete) of covariate
Statistical Analysis:	U: Unadjusted analysis
	A: Adjusted analysis
Statistical Methods:	CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
	LR: Logistic regression analysis
	PR: Polytomous logistic regression analysis

Four models were examined for each dependent variable given in Table 11-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for covariates. These covariates are given in Table 11-1. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. In an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-4, the median level of exposure to dioxin was highest for enlisted groundcrew, followed by enlisted flyers, then officers.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the CDC using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in ppt on a lipid weight basis (45). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2. A statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model to account for body mass index-related differences in elimination rate (46).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were

formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. Another category was examined by combining the low and high Ranch Hand categories. This combination is referred to in the tables as the "low plus high Ranch Hand" category. These five categories—Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the four Ranch Hand categories and the dependent variable in the Comparison category was examined. As in Model 2, a statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables. One Ranch Hand without a dioxin measure was excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The term "unadjusted" was used in the text and tables as follows: Models 1 and 4 did not adjust for any covariates. Models 2 and 3 adjusted only for body mass index at the time of the blood measurement for dioxin. The term "adjusted" was used in the text and tables as follows: Models 1 and 4 adjusted for the covariates shown in Table 11-1 unless otherwise specified by a footnote to the table. Models 2 and 3 additionally adjusted only for body mass index at the time of the blood measurement for dioxin.

Table 11-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants that were excluded from analyses is given.

Table 11-2. Number of Participants Excluded or with Missing Data for the Neurology Assessment

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Smell	DEP	1	1	0	1	1	1
Visual Fields	DEP	5	13	0	5	5	13
Light Reaction	DEP	2	4	3	2	2	4
Ocular Movement	DEP	2	3	0	2	2	3
Facial Sensation	DEP	1	0	0	1	1	0
Corneal Reflex	DEP	2	7	0	2	2	7
Jaw Clench	DEP	1	0	0	1	1	0
Smile	DEP	1	0	0	1	1	0
Palpebral Fissure	DEP	1	1	0	1	1	1
Balance	DEP	2	2	0	2	2	2
Gag Reflex	DEP	1	0	0	1	1	0
Speech	DEP	1	0	0	1	1	0
Tongue Position Relative to Midline	DEP	1	0	0	1	1	0
Palate and Uvula Movement	DEP	1	0	0	1	1	0
Shoulder Shrug	DEP	1	0	0	1	1	0

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Cranial Nerve Index	DEP	6	12	2	6	6	12
Pinprick	DEP	3	1	1	3	3	1
Light Touch	DEP	3	1	1	3	3	1
Muscle Status	DEP	6	1	1	6	6	1
Patellar Reflex	DEP	3	3	1	3	3	3
Achilles Reflex	DEP	1	0	0	1	1	0
Biceps Reflex	DEP	1	1	0	1	1	1
Babinski Reflex	DEP	2	5	0	2	2	5
Any Symmetrical Peripheral Abnormality	DEP	2	2	0	2	2	2
Possible Peripheral Neuropathy	DEP	2	1	0	2	2	1
Probable Peripheral Neuropathy	DEP	2	1	1	2	2	1
Tremor	DEP	1	0	0	1	1	0
Coordination	DEP	4	1	2	4	4	1
Romberg Sign	DEP	2	2	0	2	2	2
Gait	DEP	1	1	0	1	1	1
CNS Index	DEP	1	0	0	1	1	0
Body Mass Index	COV	1	0	0	1	1	0
Lifetime Alcohol History	COV	4	5	3	4	4	5
Composite Exposure to Heavy Metals	COV	3	7	2	3	3	7
Worked with Vibrating Power Equipment or Tools	COV	2	2	1	2	2	2
Syphilis	EXC	0	4	0	0	0	4
Tested Positive for HIV	EXC	3	2	3	3	3	2
Pre-SEA Inflammatory Disease	EXC	0	8	0	0	0	8
Pre-SEA Peripheral Disorders	EXC	3	3	0	3	2	3
Pre-SEA Other Neurological Disorders	EXC	2	3	0	2	2	3
Peripheral Edema of the Lower Extremities	EXC	136	185	88	136	136	185
Clonus of the Patellar Reflex	EXC	1	2	0	1	1	2
Clonus of the Achilles Reflex	EXC	1	4	0	1	1	4
Quadraplegia, Paraplegia, Injuries, Amputations, or Alcohol-related Disorders	EXC	23	38	9	23	23	38

[a]777 Ranch Hands and 1,174 Comparisons for group.
[b]424 Ranch Hands for initial dioxin; 776 Ranch Hands for 1987 dioxin.
[c]776 Ranch Hands and 1,174 Comparisons for categorized dioxin.

Note: DEP = Dependent variable.
   COV = Covariate.
   EXC = Exclusion.

11.2 RESULTS

11.2.1 Dependent Variable-covariate Associations

The neurology dependent variables were tested for associations with each of the covariates used in the adjusted analyses. The complete results are presented in Appendix F, Table F-3. These associations were pairwise between the dependent variable and the covariate and were not adjusted for any other covariates. A brief summary of the pattern of significant ($p \leq 0.05$) dependent variable-covariate associations is described in the following paragraphs.

Older participants were more likely to be afflicted with the following neurological disorders or abnormalities than younger participants: hereditary and degenerative diseases, peripheral disorders, other neurological disorders, balance, cranial nerve index, pinprick, light touch, patellar reflex, Achilles reflex, and biceps reflex, any symmetrical peripheral abnormality, possible peripheral neuropathy, probable peripheral neuropathy, coordination, Romberg sign, gait, and CNS index.

Blacks were more likely to have had other neurological disorders and an abnormal Babinski reflex than non-Blacks.

More enlisted flyers had other neurological disorders, followed by enlisted groundcrew, then officers. Enlisted flyers had a higher prevalence of sluggish and absent Achilles reflex, followed by officers, then enlisted groundcrew.

For the patellar reflex, nondrinkers had the smallest percentage of active or very active reflexes and the highest percentage of absent patellar reflexes. Heavy drinkers (greater than 40 drink-years), however, had the lowest percentage of active or very active Achilles and biceps reflexes. Moderate drinkers (no more than 40 drink-years) had a lower prevalence of any symmetrical peripheral abnormality and possible peripheral neuropathy. Nondrinkers had a higher prevalence of coordination and CNS index abnormalities.

Obese participants were more likely to have peripheral disorders and peripheral neuropathies than participants who were not obese. Reflexes were more likely to be absent, sluggish, or abnormal (for the Babinski reflex) in obese participants than in participants who were not obese.

Participants exposed to insecticides were more likely to have had other neurological disorders and an abnormal muscle status than participants not exposed to insecticides. Participants with exposure to degreasing chemicals had a higher prevalence of other neurological disorders than participants not exposed to degreasing chemicals. The same pattern was seen for exposure to industrial chemicals. More participants with industrial chemical exposure had an active or very active Achilles reflex than those not exposed.

Diabetic class was associated with hereditary and degenerative diseases, peripheral disorders, and other neurological disorders. Of the 15 cranial nerve function variables, diabetic class was associated with smile and balance. All peripheral nerve status variables except the Babinski reflex, and all CNS coordination processes except tremor, were associated with diabetic class. Increasing abnormalities were seen with increasing diabetic impairment for each of those variables, except smile. Diabetics had an abnormal smile most frequently, followed by participants with normal glucose levels and then by glucose-impaired participants. For the patellar, Achilles, and biceps reflexes, the percentage of absent reflexes increased as diabetic impairment increased, and the percentage of sluggish reflexes increased with diabetic impairment for the patellar and biceps reflexes.

Duration of diabetes was associated with the hereditary and degenerative diseases, peripheral disorders, and other neurological disorders. Of the 15 cranial nerve function variables, duration of diabetes was associated with visual fields, smile, balance, shoulder shrug, and the cranial nerve index. All peripheral nerve status variables, except the Babinski reflex, and all CNS coordination processes, except tremor, were associated with duration of diabetes. More abnormalities were seen in each of these variables for participants with a history of diabetes than nondiabetic or newly diagnosed participants. For the patellar, Achilles and biceps reflexes, the percentage of absent reflexes was greater for previously diagnosed diabetics than nondiabetics or newly diagnosed diabetics, and the percentage of sluggish reflexes was greater in participants with a history of diabetes for patellar and biceps reflexes.

No significant associations were seen between the peripheral abnormality or neuropathy variables and composite exposure to heavy metals or working with power equipment or tools.

11.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 11-1. Dependent variables are grouped into two sections: (1) the questionnaire variables, derived from the questionnaire that was administered during the 2002 follow-up and previous AFHS examinations, and (2) variables obtained during the 2002 physical examination.

11.2.2.1 Medical Records Variables

11.2.2.1.1 Inflammatory Diseases

No significant associations were seen between inflammatory diseases and either group or dioxin in Model 1 through Model 4 unadjusted and adjusted analyses (Table 11-3 (a-h): p>0.06 for all analyses).

Table 11-3. Analysis of Inflammatory Diseases

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*774*	*9 (1.2)*	*1.94 (0.72,5.23)*	*0.188*
	Comparison	*1,161*	*7 (0.6)*		
Officer	Ranch Hand	307	3 (1.0)	4.50 (0.47,43.46)	0.194
	Comparison	457	1 (0.2)		
Enlisted Flyer	Ranch Hand	133	2 (1.5)	2.75 (0.25,30.63)	0.411
	Comparison	181	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	334	4 (1.2)	1.26 (0.33,4.71)	0.736
	Comparison	523	5 (1.0)		

Table 11-3. Analysis of Inflammatory Diseases (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,925*	*2.43 (0.87,6.74)*	*0.088*
Officer	763	5.34 (0.55,52.27)	0.150
Enlisted Flyer	311	2.91 (0.25,33.21)	0.390
Enlisted Groundcrew	851	1.67 (0.43,6.45)	0.460

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	1 (0.7)	1.03 (0.49,2.16)	0.943
Medium	143	2 (1.4)		
High	138	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	1.01 (0.45,2.23)	0.989

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, cumulative degreasing chemical exposure, cumulative industrial chemical exposure, diabetic class, or duration of diabetes because of the sparse number of Ranch Hands with a history of inflammatory diseases.

Table 11-3. Analysis of Inflammatory Diseases (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,161	7 (0.6)		
Background RH	352	5 (1.4)	2.23 (0.70,7.15)	0.176
Low RH	211	2 (0.9)	1.60 (0.33,7.76)	0.560
High RH	210	2 (1.0)	1.68 (0.34,8.18)	0.523
Low plus High RH	421	4 (1.0)	1.64 (0.48,5.64)	0.435

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,156		
Background RH	350	3.09 (0.92,10.34)	0.068
Low RH	210	1.97 (0.39,9.97)	0.414
High RH	208	1.74 (0.34,8.87)	0.506
Low plus High RH	418	1.85 (0.52,6.60)	0.344

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	2 (0.8)	0.93 (0.61,1.41)	0.727
Medium	258	5 (1.9)		
High	255	2 (0.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 11-3. Analysis of Inflammatory Diseases (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
768	0.93 (0.58,1.48)	0.750

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race or duration of diabetes because of the sparse number of Ranch Hands with a history of inflammatory diseases.

11.2.2.1.2 *Hereditary and Degenerative Diseases*

No significant associations were seen between hereditary and degenerative diseases and group for all participants in the Model 1 unadjusted or adjusted analyses (Table 11-4(a, b): p>0.11 for all analyses). After stratifying for military occupation, however, a significant difference between Ranch Hands and Comparisons was seen in the officer stratum for both the unadjusted and adjusted analyses (Table 11-4(a,b): Unadjusted Relative Risk [RR]=1.62, p=0.019; Adjusted RR=1.57, p=0.030). More Ranch Hand officers had hereditary and degenerative diseases (18.6%) than Comparison officers (12.4%). No significant differences were detected in the unadjusted or adjusted analyses of the enlisted flyer or enlisted groundcrew strata (Table 11-4(a,b): p>0.24 for all analyses).

The Model 2 through Model 4 unadjusted and adjusted analyses showed no significant association between hereditary and degenerative diseases and dioxin (Table 11-4(c-h): p>0.15 for all analyses).

Table 11-4. Analysis of Hereditary and Degenerative Diseases

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*774*	*128 (16.5)*	*1.22 (0.95,1.57)*	*0.118*
	Comparison	*1,169*	*163 (13.9)*		
Officer	Ranch Hand	307	57 (18.6)	1.62 (1.08,2.41)	0.019*
	Comparison	461	57 (12.4)		
Enlisted Flyer	Ranch Hand	133	27 (20.3)	1.41 (0.79,2.53)	0.248
	Comparison	183	28 (15.3)		
Enlisted Groundcrew	Ranch Hand	334	44 (13.2)	0.87 (0.58,1.29)	0.491
	Comparison	525	78 (14.9)		

*: Statistically significant (0.010<p-value≤0.050).

Table 11-4. Analysis of Hereditary and Degenerative Diseases (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,933*	*1.20 (0.92,1.56)*	*0.173*
Officer	767	1.57 (1.04,2.36)	0.030*
Enlisted Flyer	313	1.40 (0.77,2.56)	0.266
Enlisted Groundcrew	853	0.85 (0.57,1.29)	0.455

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	23 (16.4)	0.97 (0.80,1.18)	0.762
Medium	143	27 (18.9)		
High	138	19 (13.8)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	1.06 (0.83,1.36)	0.654

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,169	163 (13.9)		
Background RH	352	59 (16.8)	1.26 (0.91,1.75)	0.168
Low RH	211	35 (16.6)	1.22 (0.82,1.82)	0.323
High RH	210	34 (16.2)	1.18 (0.79,1.77)	0.426
Low plus High RH	421	69 (16.4)	1.20 (0.88,1.63)	0.244

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,164		
Background RH	350	1.28 (0.91,1.80)	0.158
Low RH	210	1.15 (0.76,1.73)	0.510
High RH	208	1.13 (0.73,1.75)	0.572
Low plus High RH	418	1.14 (0.83,1.58)	0.424

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	41 (15.8)	0.98 (0.87,1.10)	0.752
Medium	258	45 (17.4)		
High	255	42 (16.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (1987 Dioxin) | |
| | **Adjusted Relative Risk** | |
n	**(95% C.I.)[a]**	**p-Value**
768	1.00 (0.86,1.16)	0.961

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.1.3 Peripheral Disorders

The Model 1 through Model 4 unadjusted and adjusted analyses showed no significant relation between peripheral disorders and either group or dioxin (Table 11-5 (a-h): p>0.07 for all analyses).

Table 11-5. Analysis of Peripheral Disorders

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*211 (27.4)*	*1.06 (0.87,1.31)*	*0.556*
	Comparison	*1,166*	*305 (26.2)*		
Officer	Ranch Hand	306	90 (29.4)	1.22 (0.88,1.68)	0.232
	Comparison	459	117 (25.5)		
Enlisted Flyer	Ranch Hand	132	38 (28.8)	1.01 (0.62,1.66)	0.967
	Comparison	182	52 (28.6)		
Enlisted Groundcrew	Ranch Hand	333	83 (24.9)	0.95 (0.69,1.30)	0.748
	Comparison	525	136 (25.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,927*	*1.03 (0.83,1.28)*	*0.795*
Officer	764	1.19 (0.85,1.68)	0.310
Enlisted Flyer	311	0.92 (0.55,1.55)	0.758
Enlisted Groundcrew	852	0.93 (0.67,1.31)	0.696

Table 11-5. Analysis of Peripheral Disorders (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	43 (30.7)	0.99 (0.85,1.17)	0.942
Medium	143	43 (30.1)		
High	138	38 (27.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	0.99 (0.81,1.22)	0.921

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,166	305 (26.2)		
Background RH	350	87 (24.9)	1.02 (0.77,1.35)	0.874
Low RH	211	65 (30.8)	1.23 (0.89,1.70)	0.214
High RH	210	59 (28.1)	1.02 (0.73,1.42)	0.920
Low plus High RH	421	124 (29.5)	1.12 (0.87,1.44)	0.383

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-5. Analysis of Peripheral Disorders (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,161		
Background RH	348	1.04 (0.77,1.40)	0.802
Low RH	210	1.10 (0.78,1.55)	0.603
High RH	208	0.96 (0.66,1.38)	0.815
Low plus High RH	418	1.02 (0.78,1.34)	0.860

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	63 (24.3)	1.09 (0.99,1.21)	0.072
Medium	257	73 (28.4)		
High	255	75 (29.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
766	1.06 (0.93,1.20)	0.407

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.1.4 Other Neurological Disorders

The Model 1 and Model 2 unadjusted and adjusted analyses showed no significant association between other neurological diseases and either group or dioxin (Table 11-6(a-d): p>0.06 for all analyses).

The unadjusted analysis of Model 3 showed significant associations between other neurological diseases and categorized dioxin for Ranch Hands in the high dioxin category (Table 11-6(e): Unadjusted RR=1.65, p=0.005) and Ranch Hands in the low and high dioxin categories combined (Table 11-6(e): Unadjusted RR=1.53, p=0.002). After adjusting for covariates, however, neither association was significant (Table 11-6(f): p>0.18 for all contrasts).

The Model 4 unadjusted analysis showed a significant relation between other neurological diseases and 1987 dioxin levels (Table 11-6(g): Unadjusted RR=1.16, p=0.007). After adjusting for covariates, the relation was not significant (Table 11-6(h): p=0.532).

Table 11-6. Analysis of Other Neurological Disorders

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*152 (19.7)*	*1.20 (0.95,1.51)*	*0.131*
	Comparison	*1,166*	*198 (17.0)*		
Officer	Ranch Hand	306	24 (7.8)	0.89 (0.53,1.52)	0.676
	Comparison	460	40 (8.7)		
Enlisted Flyer	Ranch Hand	133	44 (33.1)	1.60 (0.97,2.63)	0.065
	Comparison	182	43 (23.6)		
Enlisted Groundcrew	Ranch Hand	333	84 (25.2)	1.20 (0.87,1.66)	0.268
	Comparison	524	115 (21.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,928*	*1.16 (0.90,1.50)*	*0.239*
Officer	765	0.84 (0.49,1.44)	0.531
Enlisted Flyer	312	1.43 (0.85,2.40)	0.181
Enlisted Groundcrew	851	1.22 (0.87,1.72)	0.251

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	30 (21.4)	1.07 (0.91,1.27)	0.403
Medium	143	35 (24.5)		
High	138	34 (24.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 11-6. Analysis of Other Neurological Disorders (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	1.05 (0.85,1.29)	0.664

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,166	198 (17.0)		
Background RH	350	52 (14.9)	0.83 (0.59,1.16)	0.274
Low RH	211	47 (22.3)	1.41 (0.99,2.02)	0.060
High RH	210	52 (24.8)	1.65 (1.16,2.34)	0.005**
Low plus High RH	421	99 (23.5)	1.53 (1.16,2.01)	0.002**

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,161		
Background RH	348	1.03 (0.72,1.48)	0.873
Low RH	210	1.18 (0.80,1.73)	0.417
High RH	208	1.27 (0.87,1.85)	0.217
Low plus High RH	418	1.22 (0.91,1.64)	0.186

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-6. Analysis of Other Neurological Disorders (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
Low	258	39 (15.1)	1.16 (1.04,1.30)	0.007**
Medium	258	47 (18.2)		
High	255	65 (25.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
766	1.04 (0.91,1.20)	0.532

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.2 Physical Examination Variables – Cranial Nerve Function

Many of the cranial nerve function variables had a sparse number of abnormalities. Therefore, analysis
may have been limited, and analyses may not be adjusted for certain covariates (in particular, race,
because of the sparse number of Black participants in the AFHS). Footnotes are provided with the
subsequent tables to indicate where analysis was limited or covariates were not included in the adjusted
analysis.

11.2.2.2.1 Smell

No significant associations between group and smell were seen in the Model 1 unadjusted and adjusted
analyses (Table 11-7(a,b): p>0.16 for all analyses).

An inverse association between smell and initial dioxin was seen in the Model 2 analyses, both with and
without adjustment for covariates (Table 11-7(c,d): Unadjusted RR=0.38, p=0.012; Adjusted RR=0.30,
p=0.007). Ranch Hands in the low initial dioxin category were more likely to have an abnormal sense of
smell (3.6%) than Ranch Hands in the medium initial dioxin category (2.1%) or Ranch Hands in the high
initial dioxin category (0.0%).

The unadjusted and adjusted Model 3 analyses showed no significant association between dioxin category
and smell (Table 11-7(e,f): p>0.05 for all analyses).

A significant inverse association was seen between smell and 1987 dioxin levels in the unadjusted and adjusted Model 4 analyses (Table 11-7(g,h): Unadjusted RR=0.71, p=0.018; Adjusted RR=0.64, p=0.010). Abnormal sense of smell was more prevalent in Ranch Hands in the low 1987 dioxin category (4.6%), followed by the medium 1987 dioxin category (2.7%), then the high 1987 dioxin category (0.8%).

Table 11-7. Analysis of Smell

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*21 (2.7)*	*1.18 (0.66,2.10)*	*0.576*
	Comparison	*1,168*	*27 (2.3)*		
Officer	Ranch Hand	306	8 (2.6)	0.93 (0.38,2.26)	0.864
	Comparison	461	13 (2.8)		
Enlisted Flyer	Ranch Hand	133	3 (2.3)	0.82 (0.19,3.48)	0.784
	Comparison	182	5 (2.7)		
Enlisted Groundcrew	Ranch Hand	334	10 (3.0)	1.77 (0.71,4.40)	0.220
	Comparison	525	9 (1.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,932*	*1.21 (0.67,2.18)*	*0.531*
Officer	767	0.90 (0.37,2.23)	0.827
Enlisted Flyer	312	0.82 (0.19,3.56)	0.792
Enlisted Groundcrew	853	1.94 (0.77,4.87)	0.161

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	5 (3.6)	0.38 (0.16,0.95)	0.012*
Medium	143	3 (2.1)		
High	138	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 11-7. Analysis of Smell (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
418	0.30 (0.10,0.89)	0.007**

[a]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,168	27 (2.3)		
Background RH	351	13 (3.7)	1.72 (0.87,3.39)	0.119
Low RH	211	8 (3.8)	1.64 (0.73,3.66)	0.230
High RH	210	0 (0.0)	--	0.051[c]
Low plus High RH	421	8 (1.9)	--	0.765[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of
 participants with an abnormal sense of smell.

--: Results were not presented because of the sparse number of participants with an abnormal sense of smell.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,163		
Background RH	350	1.80 (0.89,3.64)	0.103
Low RH	210	1.57 (0.69,3.57)	0.286
High RH	208	--	--
Low plus High RH	418	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with an abnormal sense of smell.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-7. Analysis of Smell (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	12 (4.6)	0.71 (0.53,0.95)	0.018*
Medium	258	7 (2.7)		
High	255	2 (0.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	0.64 (0.45,0.90)	0.010**

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

11.2.2.2.2 Visual Fields

In the Model 1 unadjusted and adjusted analyses of all participants, Ranch Hands were significantly more likely to have abnormal visual fields than Comparisons (Table 11-8(a,b): Unadjusted RR=2.60, p=0.040; Adjusted RR=3.08, p=0.022). Abnormal visual fields were seen in 1.6 percent of Ranch Hands compared to 0.6 percent of Comparisons. When stratified by military occupation, no significant associations were seen in the unadjusted or adjusted analyses (Table 11-8(a,b): p>0.05 for all contrasts).

No significant associations were seen between visual fields and initial dioxin in Model 2 unadjusted and adjusted analyses (Table 11-8(c,d): p>0.67 for both analyses).

In the Model 3 unadjusted and adjusted analyses, a significant association was seen between categorized dioxin and visual fields for the background dioxin category (Table 11-8(e,f): Unadjusted RR=4.37, p=0.005; Adjusted RR=5.25, p=0.004). Abnormal visual fields were seen in 2.3 percent of Ranch Hands in the background dioxin category compared to 0.6 percent of Comparisons. No other unadjusted or adjusted Model 3 contrast showed a significant association (Table 11-8(e,f): p>0.44 for all contrasts).

No significant association was seen between visual fields and 1987 dioxin levels in the Model 4 unadjusted and adjusted analyses (Table 11-8(g,h): p>0.10 for all analyses).

Table 11-8. Analysis of Visual Fields

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*769*	*12 (1.6)*	*2.60 (1.02,6.64)*	*0.040**
	Comparison	*1,157*	*7 (0.6)*		
Officer	Ranch Hand	303	6 (2.0)	4.62 (0.93,23.02)	0.062
	Comparison	459	2 (0.4)		
Enlisted Flyer	Ranch Hand	133	3 (2.3)	4.15 (0.43,40.39)	0.220
	Comparison	181	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	333	3 (0.9)	1.17 (0.26,5.24)	0.841
	Comparison	517	4 (0.8)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,917*	*3.08 (1.13,8.41)*	*0.022**
Officer	762	4.88 (0.97,24.68)	0.055
Enlisted Flyer	311	--	--
Enlisted Groundcrew	844	1.20 (0.26,5.50)	0.814

--: Results were not presented because of the sparse number of participants with abnormal visual fields.

*: Statistically significant (0.010<p-value≤0.050).

Note: Results were not adjusted for race because of the sparse number of participants with abnormal visual fields.

(c) MODEL 2: RANCH HANDS − INITIAL DIOXIN − UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	2 (1.4)	0.85 (0.39,1.85)	0.676
Medium	141	0 (0.0)		
High	137	2 (1.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 11-8. Analysis of Visual Fields (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

| | Analysis Results for Log_2 (Initial Dioxin) | |
| | Adjusted Relative Risk | |
n	(95% C.I.)[a]	p-Value
415	0.98 (0.43,2.24)	0.957

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, cumulative insecticide exposure, cumulative degreasing chemical exposure, or cumulative industrial chemical exposure because of the sparse number of Ranch Hands with abnormal visual fields.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,157	7 (0.6)		
Background RH	350	8 (2.3)	4.37 (1.55,12.30)	0.005**
Low RH	209	2 (1.0)	1.51 (0.31,7.34)	0.613
High RH	209	2 (1.0)	1.41 (0.29,6.91)	0.671
Low plus High RH	418	4 (1.0)	1.46 (0.42,5.05)	0.552

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-8. Analysis of Visual Fields (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,152		
Background RH	349	5.25 (1.71,16.13)	0.004**
Low RH	208	1.61 (0.31,8.30)	0.568
High RH	207	1.72 (0.32,9.24)	0.526
Low plus High RH	415	1.67 (0.45,6.19)	0.445

[a]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

  Results were not adjusted for race because of the sparse number of participants with abnormal visual fields.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	6 (2.3)	0.75 (0.52,1.09)	0.126
Medium	256	4 (1.6)		
High	253	2 (0.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
764	0.67 (0.42,1.09)	0.109

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with abnormal visual fields.

11.2.2.2.3 Light Reaction

Light reaction was not significantly associated with group in the Model 1 analyses or dioxin in the Model 3 or Model 4 unadjusted and adjusted analyses (Table 11-9(a,b,e-h): p>0.47 for all analyses).

In the unadjusted Model 2 analyses, a significant association was seen between initial dioxin and light reaction (Table 11-9(c): Unadjusted RR=3.98, p=0.039). After adjusting for covariates, however, the association was no longer significant (Table 11-9(d): p=0.057).

Table 11-9. Analysis of Light Reaction

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*4 (0.5)*	*0.75 (0.23,2.51)*	*0.640*
	Comparison	*1,165*	*8 (0.7)*		
Officer	Ranch Hand	306	1 (0.3)	0.75 (0.07,8.33)	0.817
	Comparison	461	2 (0.4)		
Enlisted Flyer	Ranch Hand	132	0 (0.0)	--	--
	Comparison	182	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	334	3 (0.9)	0.78 (0.19,3.14)	0.726
	Comparison	522	6 (1.1)		

--: Results were not presented because of the sparse number of participants with abnormal light reaction.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,928*	*0.72 (0.21,2.44)*	*0.594*
Officer	767	0.76 (0.07,8.57)	0.828
Enlisted Flyer	311	--	--
Enlisted Groundcrew	850	0.75 (0.18,3.14)	0.699

--: Results were not presented because of the sparse number of participants with abnormal light reaction.

Note: Results were not adjusted for race or military occupation in the analysis of all participants because of the sparse number of participants with an abnormal light reaction. Results were not adjusted for race in the occupational category analyses because of the sparse number of participants with an abnormal light reaction.

Table 11-9. Analysis of Light Reaction (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	0 (0.0)	3.98 (0.96,16.53)	0.039*
Medium	143	0 (0.0)		
High	138	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	4.09 (0.77,21.67)	0.057

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, cumulative insecticide exposure, cumulative
         degreasing chemical exposure, cumulative industrial chemical exposure, diabetic class, or duration of
         diabetes because of the sparse number of Ranch Hands with an abnormal light reaction.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,165	8 (0.7)		
Background RH	350	3 (0.9)	1.12 (0.29,4.31)	0.865
Low RH	211	0 (0.0)	--	0.475[c]
High RH	210	1 (0.5)	0.76 (0.09,6.18)	0.800
Low plus High RH	421	1 (0.2)	--	0.501[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of
 participants with an abnormal light reaction.

--: Results were not presented because of the sparse number of participants with abnormal light reaction.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-9. Analysis of Light Reaction (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,160		
Background RH	349	1.11 (0.29,4.35)	0.877
Low RH	210	--	--
High RH	208	0.79 (0.10,6.63)	0.832
Low plus High RH	418	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with abnormal light reaction.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race or military occupation because of the sparse number of participants with an abnormal light reaction.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	258	3 (1.2)	1.01 (0.55,1.87)	0.971
Medium	258	0 (0.0)		
High	255	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
767	1.15 (0.59,2.24)	0.692

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, military occupation, cumulative insecticide exposure, diabetic class, or duration of diabetes because of the sparse number of Ranch Hands with an abnormal light reaction.

11.2.2.2.4 Ocular Movement

No significant association between ocular movement and group or dioxin was seen in the Model 1 through Model 4 unadjusted and adjusted analyses (Table 11-10 (a-h): p>0.18 for all analyses).

Table 11-10. Analysis of Ocular Movement

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*5 (0.6)*	*1.89 (0.51,7.07)*	*0.341*
	Comparison	*1,166*	*4 (0.3)*		
Officer	Ranch Hand	306	2 (0.7)	1.51 (0.21,10.78)	0.681
	Comparison	461	2 (0.4)		
Enlisted Flyer	Ranch Hand	132	1 (0.8)	--	0.872[a]
	Comparison	182	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	334	2 (0.6)	1.57 (0.22,11.19)	0.653
	Comparison	523	2 (0.4)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal ocular movement.

--: Results were not presented because of the sparse number of participants with abnormal ocular movement.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,929*	*2.21 (0.57,8.52)*	*0.248*
Officer	767	1.74 (0.24,12.70)	0.587
Enlisted Flyer	311	--	--
Enlisted Groundcrew	851	1.92 (0.26,14.08)	0.519

--: Results were not presented because of the sparse number of participants with abnormal ocular movement.

Note: Results were not adjusted for race because of the sparse number of participants with abnormal ocular movement.

Table 11-10. Analysis of Ocular Movement (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Abnormal**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	140	1 (0.7)	0.82 (0.28,2.42)	0.712
Medium	143	0 (0.0)		
High	138	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
418	0.19 (0.01,5.66)	0.189

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, cumulative insecticide exposure, cumulative degreasing chemical exposure, cumulative industrial chemical exposure, diabetic class, or duration of diabetes because of the sparse number of Ranch Hands with abnormal ocular movement.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,166	4 (0.3)		
Background RH	350	3 (0.9)	2.69 (0.59,12.28)	0.201
Low RH	211	1 (0.5)	1.35 (0.15,12.16)	0.789
High RH	210	1 (0.5)	1.31 (0.14,11.85)	0.813
Low plus High RH	421	2 (0.5)	1.33 (0.24,7.32)	0.745

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-10. Analysis of Ocular Movement (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,161		
Background RH	349	2.94 (0.60,14.47)	0.185
Low RH	210	1.72 (0.18,16.14)	0.633
High RH	208	1.31 (0.11,16.31)	0.834
Low plus High RH	418	1.50 (0.24,9.36)	0.662

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Note: Results were not adjusted for race because of the sparse number of participants with abnormal ocular movement.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	258	3 (1.2)	0.91 (0.52,1.60)	0.746
Medium	258	1 (0.4)		
High	255	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
767	0.96 (0.48,1.92)	0.912

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, cumulative industrial chemical exposure, diabetic class, or duration of diabetes because of the sparse number of Ranch Hands with abnormal ocular movement.

11.2.2.2.5 Facial Sensation

Facial sensation was not significantly associated with group in the Model 1 unadjusted and adjusted analyses or dioxin in the Model 2 and 4 unadjusted and adjusted analyses (Table 11-11(a-d,g,h): p>0.24 for all analyses).

In the Model 3 unadjusted and adjusted analyses, a significant difference in abnormal facial sensation was seen between Ranch Hands in the low dioxin category and Comparisons (Table 11-11(e,f): Unadjusted RR=5.74, p=0.033; Adjusted RR=7.94, p=0.033). Ranch Hands in the low category were more likely to have abnormal facial sensation (1.4%) than Comparisons (0.3%). No other unadjusted or adjusted Model 3 contrasts were significant (Table 11-11(e,f): p>0.39 for each analysis).

Table 11-11. Analysis of Facial Sensation

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*4 (0.5)*	*2.02 (0.45,9.06)*	*0.354*
	Comparison	*1,169*	*3 (0.3)*		
Officer	Ranch Hand	306	1 (0.3)	1.51 (0.09,24.20)	0.772
	Comparison	461	1 (0.2)		
Enlisted Flyer	Ranch Hand	133	1 (0.8)	0.69 (0.06,7.64)	0.759
	Comparison	183	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	334	2 (0.6)	--	0.294[a]
	Comparison	525	0 (0.0)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal facial sensation.

--: Results were not presented because of the sparse number of participants with abnormal facial sensation.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,933*	*2.74 (0.48,15.76)*	*0.244*
Officer	767	1.31 (0.08,21.52)	0.850
Enlisted Flyer	313	1.06 (0.06,19.00)	0.969
Enlisted Groundcrew	853	--	--

--: Results were not presented because of the sparse number of participants with abnormal facial sensation.

Note: Results were not adjusted for diabetic class because of the sparse number of participants with abnormal facial sensation.

Table 11-11. Analysis of Facial Sensation (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Abnormal**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	140	2 (1.4)	0.59 (0.17,2.05)	0.359
Medium	143	1 (0.7)		
High	138	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
418	0.43 (0.08,2.40)	0.276

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for military occupation, cumulative insecticide exposure, cumulative degreasing chemical exposure, cumulative industrial chemical exposure, diabetic class, or duration of diabetes because of the sparse number of Ranch Hands with abnormal facial sensation.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,169	3 (0.3)		
Background RH	351	1 (0.3)	0.99 (0.10,9.64)	0.993
Low RH	211	3 (1.4)	5.74 (1.15,28.69)	0.033*
High RH	210	0 (0.0)	--	0.999[c]
Low plus High RH	421	3 (0.7)	--	0.398[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with abnormal facial sensation.

--: Results were not presented because of the sparse number of participants with abnormal facial sensation.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-11. Analysis of Facial Sensation (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,164		
Background RH	350	1.33 (0.11,15.68)	0.823
Low RH	210	7.94 (1.19,53.10)	0.033*
High RH	208	--	--
Low plus High RH	418	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with abnormal facial sensation.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for diabetic class because of the sparse number of participants with abnormal facial sensation.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	1 (0.4)	0.99 (0.53,1.83)	0.967
Medium	258	2 (0.8)		
High	255	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	1.17 (0.57,2.40)	0.677

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for cumulative insecticide exposure, diabetic class, or duration of diabetes because of the sparse number of Ranch Hands with abnormal facial sensation.

11.2.2.2.6 Corneal Reflex

Corneal reflex was not significantly associated with group or dioxin in the Model 1 through Model 4 unadjusted and adjusted analyses (Table 11-12(a-h): p>0.47 for all analyses).

Table 11-12. Analysis of Corneal Reflex

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*2 (0.3)*	*0.60 (0.12,3.11)*	*0.530*
	Comparison	*1,162*	*5 (0.4)*		
Officer	Ranch Hand	306	1 (0.3)	0.75 (0.07,8.33)	0.817
	Comparison	461	2 (0.4)		
Enlisted Flyer	Ranch Hand	133	0 (0.0)	--	0.999[a]
	Comparison	181	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	333	1 (0.3)	0.78 (0.07,8.64)	0.840
	Comparison	520	2 (0.4)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal corneal reflex.

--: Results were not presented because of the sparse number of participants with an abnormal corneal reflex.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,925*	*0.55 (0.10,3.00)*	*0.479*
Officer	767	0.78 (0.07,9.04)	0.845
Enlisted Flyer	311	--	--
Enlisted Groundcrew	847	0.69 (0.06,8.16)	0.771

--: Results were not presented because of the sparse number of participants with an abnormal corneal reflex.

Note: Results were not adjusted for race because of the sparse number of participants with an abnormal corneal reflex.

Table 11-12. Analysis of Corneal Reflex (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	0 (0.0)	1.17 (0.24,5.76)	0.853
Medium	143	1 (0.7)		
High	138	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	0.73 (0.03,15.84)	0.831

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, cumulative insecticide exposure, cumulative
degreasing chemical exposure, cumulative industrial chemical exposure, diabetic class, or duration of
diabetes because of the sparse number of Ranch Hands with an abnormal corneal reflex.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,162	5 (0.4)		
Background RH	350	1 (0.3)	0.56 (0.06,4.86)	0.598
Low RH	211	0 (0.0)	--	0.739[c]
High RH	210	1 (0.5)	1.30 (0.15,11.38)	0.811
Low plus High RH	421	1 (0.2)	--	0.929[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of
  participants with an abnormal corneal reflex.

--: Results were not presented because of the sparse number of participants with an abnormal corneal reflex.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-12. Analysis of Corneal Reflex (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,157		
Background RH	349	0.55 (0.06,5.01)	0.598
Low RH	210	--	--
High RH	208	1.22 (0.11,12.96)	0.869
Low plus High RH	418	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with an abnormal corneal reflex.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Note: Results were not adjusted for race because of the sparse number of participants with an abnormal corneal reflex.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	1 (0.4)	1.01 (0.43,2.39)	0.984
Medium	257	0 (0.0)		
High	255	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
767	1.07 (0.48,2.41)	0.862

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, military occupation, cumulative insecticide exposure, cumulative industrial chemical exposure, diabetic class, or duration of diabetes because of the sparse number of Ranch Hands with an abnormal corneal reflex.

11.2.2.2.7 Jaw Clench

Only two participants, a non-Black Comparison officer and a non-Black Comparison enlisted groundcrew, had a deviated jaw clench, which precluded statistical analysis.

11.2.2.2.8 Smile

No significant association between smile and group or dioxin was seen in the Model 1 through Model 4 unadjusted and adjusted analyses (Table 11-13(a-h): p>0.28 for all analyses).

Table 11-13. Analysis of Smile

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*8 (1.0)*	*1.10 (0.44,2.75)*	*0.837*
	Comparison	*1,169*	*11 (0.9)*		
Officer	Ranch Hand	306	4 (1.3)	1.00 (0.28,3.59)	0.995
	Comparison	461	6 (1.3)		
Enlisted Flyer	Ranch Hand	133	1 (0.8)	0.69 (0.06,7.64)	0.759
	Comparison	183	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	334	3 (0.9)	1.58 (0.32,7.86)	0.578
	Comparison	525	3 (0.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,933*	*1.07 (0.40,2.88)*	*0.895*
Officer	767	0.78 (0.21,2.92)	0.708
Enlisted Flyer	313	1.01 (0.06,16.77)	0.994
Enlisted Groundcrew	853	1.99 (0.33,12.14)	0.457

Note: Results were not adjusted for race or diabetic class because of the sparse number of participants with an abnormal smile.

Table 11-13. Analysis of Smile (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	2 (1.4)	0.85 (0.45,1.59)	0.593
Medium	143	3 (2.1)		
High	138	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	0.86 (0.40,1.83)	0.686

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, cumulative insecticide exposure, or diabetic class because of the sparse number of Ranch Hands with an abnormal smile.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,169	11 (0.9)		
Background RH	351	2 (0.6)	0.70 (0.15,3.20)	0.647
Low RH	211	4 (1.9)	1.90 (0.59,6.07)	0.281
High RH	210	2 (1.0)	0.87 (0.19,4.02)	0.862
Low plus High RH	421	6 (1.4)	1.29 (0.45,3.68)	0.636

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-13. Analysis of Smile (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,164		
Background RH	350	0.58 (0.12,2.86)	0.506
Low RH	210	1.78 (0.51,6.17)	0.367
High RH	208	1.20 (0.22,6.40)	0.833
Low plus High RH	418	1.46 (0.46,4.62)	0.521

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Note: Results were not adjusted for race or diabetic class because of the sparse number of participants with an abnormal smile.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	2 (0.8)	1.17 (0.77,1.77)	0.479
Medium	258	3 (1.2)		
High	255	3 (1.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	1.13 (0.63,2.03)	0.681

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, cumulative insecticide exposure, or diabetic class because of the sparse number of Ranch Hands with an abnormal smile.

11.2.2.2.9 Palpebral Fissure

The Model 1 through Model 4 unadjusted and adjusted analyses showed no significant association between palpebral fissure and group or dioxin (Table 11-14(a-h): p>0.14 for all analyses).

Table 11-14. Analysis of Palpebral Fissure

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*23 (3.0)*	*1.53 (0.85,2.74)*	*0.158*
	Comparison	*1,168*	*23 (2.0)*		
Officer	Ranch Hand	306	9 (2.9)	1.37 (0.55,3.40)	0.502
	Comparison	461	10 (2.2)		
Enlisted Flyer	Ranch Hand	133	5 (3.8)	1.15 (0.34,3.86)	0.818
	Comparison	183	6 (3.3)		
Enlisted Groundcrew	Ranch Hand	334	9 (2.7)	2.05 (0.75,5.55)	0.160
	Comparison	524	7 (1.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,932*	*1.57 (0.86,2.87)*	*0.143*
Officer	767	1.36 (0.54,3.41)	0.514
Enlisted Flyer	313	1.31 (0.37,4.67)	0.680
Enlisted Groundcrew	852	2.09 (0.76,5.73)	0.151

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	4 (2.9)	1.07 (0.70,1.62)	0.762
Medium	143	3 (2.1)		
High	138	5 (3.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 11-14. Analysis of Palpebral Fissure (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
418	1.51 (0.86,2.65)	0.155

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,168	23 (2.0)		
Background RH	351	11 (3.1)	1.66 (0.79,3.45)	0.179
Low RH	211	7 (3.3)	1.69 (0.72,4.00)	0.229
High RH	210	5 (2.4)	1.19 (0.44,3.17)	0.734
Low plus High RH	421	12 (2.9)	1.42 (0.69,2.90)	0.339

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,163		
Background RH	350	1.66 (0.77,3.55)	0.193
Low RH	210	1.62 (0.67,3.92)	0.285
High RH	208	1.36 (0.48,3.82)	0.559
Low plus High RH	418	1.49 (0.70,3.13)	0.299

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-14. Analysis of Palpebral Fissure (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Abnormal**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	259	10 (3.9)	1.01 (0.78,1.31)	0.926
Medium	258	6 (2.3)		
High	255	7 (2.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
768	1.00 (0.73,1.39)	0.981

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.2.10 Balance

No significant associations were seen between balance and group in the Model 1 unadjusted and adjusted analyses (Table 11-15(a,b): p>0.25 for all analyses).

The unadjusted analysis of Model 2 showed no association between initial dioxin levels and balance (Table 11-15(c): p=0.961). After adjusting for covariates, however, the association was significant (Table 11-15(d): Adjusted RR=2.11, p=0.033). The difference between the unadjusted and adjusted results was partially due to more balance abnormalities in officers than enlisted personnel, for Ranch Hands with an initial dioxin estimate. More Ranch Hands in the low and high initial dioxin categories had abnormal balance (2.9% for each category) than those in the medium category (2.1%).

The associations between balance and dioxin in the Model 3 and 4 unadjusted and adjusted analyses were nonsignificant (Table 11-15(e-h): p>0.12 for all analyses).

Table 11-15. Analysis of Balance

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*18 (2.3)*	*1.24 (0.66,2.33)*	*0.499*
	Comparison	*1,168*	*22 (1.9)*		
Officer	Ranch Hand	306	10 (3.3)	1.70 (0.68,4.23)	0.256
	Comparison	461	9 (2.0)		
Enlisted Flyer	Ranch Hand	133	5 (3.8)	1.39 (0.39,4.90)	0.608
	Comparison	183	5 (2.7)		
Enlisted Groundcrew	Ranch Hand	333	3 (0.9)	0.59 (0.15,2.23)	0.433
	Comparison	524	8 (1.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,931*	*1.13 (0.59,2.18)*	*0.717*
Officer	767	1.64 (0.64,4.25)	0.304
Enlisted Flyer	313	1.15 (0.31,4.19)	0.837
Enlisted Groundcrew	851	0.56 (0.14,2.18)	0.400

Note: Results were not adjusted for race because of the sparse number of participants with abnormal balance.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	4 (2.9)	1.01 (0.64,1.60)	0.961
Medium	143	3 (2.1)		
High	138	4 (2.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 11-15. Analysis of Balance (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
418	2.11 (1.03,4.34)	0.033*

[a]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with abnormal balance.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,168	22 (1.9)		
Background RH	350	7 (2.0)	1.07 (0.45,2.53)	0.886
Low RH	211	6 (2.8)	1.52 (0.61,3.81)	0.367
High RH	210	5 (2.4)	1.27 (0.47,3.40)	0.637
Low plus High RH	421	11 (2.6)	1.39 (0.67,2.90)	0.380

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,163		
Background RH	349	1.00 (0.40,2.48)	0.998
Low RH	210	1.10 (0.42,2.87)	0.841
High RH	208	1.40 (0.48,4.14)	0.538
Low plus High RH	418	1.24 (0.56,2.75)	0.590

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

        Results were not adjusted for race because of the sparse number of participants with abnormal balance.

Table 11-15. Analysis of Balance (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Abnormal**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	259	5 (1.9)	1.04 (0.78,1.39)	0.799
Medium	257	6 (2.3)		
High	255	7 (2.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
767	1.44 (0.90,2.32)	0.124

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with abnormal balance.

11.2.2.2.11   Gag Reflex

Gag reflex showed no significant relation with group or dioxin in the Model 1 through Model 4 unadjusted and adjusted analyses (Table 11-16(a-h): p>0.09 for all analyses).

Table 11-16. Analysis of Gag Reflex

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*2 (0.3)*	*3.03 (0.27,33.47)*	*0.348*
	Comparison	*1,169*	*1 (0.1)*		
Officer	Ranch Hand	306	0 (0.0)	--	--
	Comparison	461	0 (0.0)		
Enlisted Flyer	Ranch Hand	133	1 (0.8)	1.38 (0.09,22.24)	0.821
	Comparison	183	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	334	1 (0.3)	--	0.820[a]
	Comparison	525	0 (0.0)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal gag reflex.

--: Results were not presented because of the sparse number of participants with an abnormal gag reflex.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,933*	*3.09 (0.24,39.24)*	*0.367*
Officer	767	--	--
Enlisted Flyer	313	1.45 (0.04,56.04)	0.842
Enlisted Groundcrew	853	--	--

--: Results were not presented because of the sparse number of participants with an abnormal gag reflex.

Note: Results were not adjusted for race, military occupation, or cumulative insecticide exposure in the analysis of all participants because of the sparse number of participants with an abnormal gag reflex. Results were not adjusted for race or cumulative insecticide exposure in the analysis of occupational category analyses because of the sparse number of participants with an abnormal gag reflex.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	1 (0.7)	0.82 (0.20,3.35)	0.773
Medium	143	1 (0.7)		
High	138	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 11-16. Analysis of Gag Reflex (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
418	0.58 (0.09,3.82)	0.490

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, cumulative insecticide exposure, cumulative industrial chemical exposure, diabetic class, or duration of diabetes because of the sparse number of Ranch Hands with an abnormal gag reflex.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,169	1 (0.1)		
Background RH	351	0 (0.0)	--	0.999[c]
Low RH	211	1 (0.5)	5.77 (0.36,93.26)	0.217
High RH	210	1 (0.5)	7.61 (0.46,126.82)	0.158
Low plus High RH	421	2 (0.5)	6.62 (0.59,74.18)	0.125

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal gag reflex.

--:   Results were not presented because of the sparse number of participants with an abnormal gag reflex.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-16. Analysis of Gag Reflex (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,164		
Background RH	350	--	--
Low RH	210	18.43 (0.60,567.42)	0.096
High RH	208	8.50 (0.29,250.29)	0.215
Low plus High RH	418	12.54 (0.65,241.33)	0.094

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with an abnormal gag reflex.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

    Results were not adjusted for race, military occupation, or cumulative insecticide exposure in the analysis of all participants because of the sparse number of participants with an abnormal gag reflex.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	0 (0.0)	1.27 (0.56,2.88)	0.580
Medium	258	1 (0.4)		
High	255	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	1.37 (0.69,2.70)	0.376

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, military occupation, cumulative insecticide exposure, cumulative industrial chemical exposure, diabetic class, or duration of diabetes because of the sparse number of Ranch Hands with an abnormal gag reflex.

11.2.2.2.12 Speech

No significant association was seen between speech and group or dioxin in the Model 1 through Model 4 unadjusted and adjusted analyses (Tables 11-17(a-h): p≥0.21 for all analyses).

Table 11-17. Analysis of Speech

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*10 (1.3)*	*1.26 (0.54,2.94)*	*0.589*
	Comparison	*1,169*	*12 (1.0)*		
Officer	Ranch Hand	306	4 (1.3)	1.51 (0.38,6.10)	0.560
	Comparison	461	4 (0.9)		
Enlisted Flyer	Ranch Hand	133	1 (0.8)	1.38 (0.09,22.24)	0.821
	Comparison	183	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	334	5 (1.5)	1.12 (0.35,3.57)	0.842
	Comparison	525	7 (1.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,933*	*1.73 (0.69,4.30)*	*0.244*
Officer	767	1.69 (0.41,6.93)	0.469
Enlisted Flyer	313	--	--
Enlisted Groundcrew	853	1.47 (0.42,5.11)	0.545

--: Results were not presented because of the sparse number of participants with abnormal speech.

Note: Results were not adjusted for race because of the sparse number of participants with abnormal speech.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	2 (1.4)	0.76 (0.36,1.60)	0.447
Medium	143	2 (1.4)		
High	138	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 11-17. Analysis of Speech (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
418	0.92 (0.34,2.48)	0.875

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with abnormal speech.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,169	12 (1.0)		
Background RH	351	5 (1.4)	1.47 (0.51,4.25)	0.473
Low RH	211	2 (0.9)	0.91 (0.20,4.08)	0.897
High RH	210	3 (1.4)	1.33 (0.37,4.78)	0.663
Low plus High RH	421	5 (1.2)	1.10 (0.38,3.19)	0.866

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,164		
Background RH	350	1.65 (0.52,5.26)	0.395
Low RH	210	1.29 (0.27,6.12)	0.750
High RH	208	2.48 (0.60,10.22)	0.210
Low plus High RH	418	1.78 (0.57,5.62)	0.323

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race because of the sparse number of participants with abnormal speech.

Table 11-17. Analysis of Speech (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	5 (1.9)	0.85 (0.57,1.26)	0.409
Medium	258	2 (0.8)		
High	255	3 (1.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	0.89 (0.54,1.49)	0.662

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with abnormal speech.

11.2.2.2.13 Tongue Position Relative to Midline

The Model 1 through Model 4 unadjusted and adjusted analyses showed no significant relation between tongue position relative to midline and group or dioxin (Table 11-18(a-h): p>0.06 for all analyses).

Table 11-18. Analysis of Tongue Position Relative to Midline

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Deviated	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*3 (0.4)*	*2.27 (0.38,13.64)*	*0.362*
	Comparison	*1,169*	*2 (0.2)*		
Officer	Ranch Hand	306	1 (0.3)	1.51 (0.09,24.20)	0.772
	Comparison	461	1 (0.2)		
Enlisted Flyer	Ranch Hand	133	1 (0.8)	1.38 (0.09,22.24)	0.821
	Comparison	183	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	334	1 (0.3)	--	0.820[a]
	Comparison	525	0 (0.0)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated tongue position relative to midline.

--: Results were not presented because of the sparse number of participants with a deviated tongue position relative to midline.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,933*	*2.22 (0.35,14.03)*	*0.390*
Officer	767	1.57 (0.09,26.03)	0.753
Enlisted Flyer	313	1.17 (0.07,19.65)	0.916
Enlisted Groundcrew	853	--	--

--: Results were not presented because of the sparse number of participants with a deviated tongue position relative to midline.

Note: Results were not adjusted for race, diabetic class, or duration of diabetes because of the sparse number of participants with a deviated tongue position relative to midline.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Deviated	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	2 (1.4)	1.05 (0.45,2.45)	0.915
Medium	143	0 (0.0)		
High	138	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	1.23 (0.36,4.24)	0.742

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, cumulative insecticide exposure, diabetic class, or duration of diabetes because of the sparse number of Ranch Hands with a deviated tongue position relative to midline.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Deviated	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,169	2 (0.2)		
Background RH	351	0 (0.0)	--	0.999[c]
Low RH	211	2 (0.9)	5.55 (0.78,39.71)	0.088
High RH	210	1 (0.5)	2.75 (0.25,30.77)	0.413
Low plus High RH	421	3 (0.7)	3.91 (0.62,24.68)	0.147

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with a deviated tongue position relative to midline.

--: Results were not presented because of the sparse number of participants with a deviated tongue position relative to midline.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-18. Analysis of Tongue Position Relative to Midline (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,164		
Background RH	350	--	--
Low RH	210	5.40 (0.69,42.33)	0.109
High RH	208	3.28 (0.22,48.44)	0.387
Low plus High RH	418	4.22 (0.57,31.00)	0.158

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with a deviated tongue position relative to midline.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

   Results were not adjusted for race, diabetic class, or duration of diabetes because of the sparse number of participants with a deviated tongue position relative to midline.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Deviated	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	0 (0.0)	1.59 (0.83,3.06)	0.172
Medium	258	2 (0.8)		
High	255	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	2.56 (0.85,7.68)	0.069

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, cumulative insecticide exposure, diabetic class, or duration of diabetes because of the sparse number of Ranch Hands with a deviated tongue position relative to midline.

11.2.2.2.14 Palate and Uvula Movement

Only two participants, a non-Black Comparison officer and a non-Black Ranch Hand enlisted flyer, had a deviated palate and uvula movement. Because of the sparse number of abnormalities, further statistical analysis was not performed.

11.2.2.2.15 Shoulder Shrug

No significant association was seen between an abnormal shoulder shrug, which was used to test cranial nerve XI, and either group or dioxin in the Model 1 through Model 4 unadjusted and adjusted analyses (Table 11-19(a-h): p>0.10 for all analyses).

Table 11-19. Analysis of Shoulder Shrug

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*3 (0.4)*	*0.76 (0.19,3.03)*	*0.688*
	Comparison	*1,169*	*6 (0.5)*		
Officer	Ranch Hand	306	2 (0.7)	1.51 (0.21,10.78)	0.681
	Comparison	461	2 (0.4)		
Enlisted Flyer	Ranch Hand	133	0 (0.0)	--	0.623[a]
	Comparison	183	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	334	1 (0.3)	0.79 (0.07,8.69)	0.844
	Comparison	525	2 (0.4)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal shoulder shrug.

--: Results were not presented because of the sparse number of participants with an abnormal shoulder shrug.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,933*	*0.92 (0.22,3.90)*	*0.909*
Officer	767	1.61 (0.22,11.81)	0.638
Enlisted Flyer	313	--	--
Enlisted Groundcrew	853	0.80 (0.07,9.06)	0.860

--: Results were not presented because of the sparse number of participants with an abnormal shoulder shrug.

Note: Results were not adjusted for cumulative insecticide exposure because of the sparse number of participants with an abnormal shoulder shrug.

Table 11-19. Analysis of Shoulder Shrug (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	2 (1.4)	0.25 (0.03,2.53)	0.127
Medium	143	0 (0.0)		
High	138	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	0.15 (0.01,3.33)	0.101

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, cumulative insecticide exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal shoulder shrug.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,169	6 (0.5)		
Background RH	351	1 (0.3)	0.64 (0.08,5.35)	0.677
Low RH	211	2 (0.9)	1.74 (0.35,8.76)	0.502
High RH	210	0 (0.0)	--	0.638[c]
Low plus High RH	421	2 (0.5)	--	0.999[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal shoulder shrug.

--: Results were not presented because of the sparse number of participants with an abnormal shoulder shrug.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-19. Analysis of Shoulder Shrug (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,164		
Background RH	350	0.70 (0.08,6.25)	0.746
Low RH	210	2.13 (0.39,11.61)	0.384
High RH	208	--	--
Low plus High RH	418	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with an abnormal shoulder shrug.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for cumulative insecticide exposure because of the sparse number of Ranch Hands with an abnormal shoulder shrug.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	0 (0.0)	0.90 (0.43,1.85)	0.764
Medium	258	3 (1.2)		
High	255	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	0.81 (0.35,1.86)	0.622

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for military occupation, cumulative insecticide exposure, and diabetic class because of the sparse number of Ranch Hands with an abnormal shoulder shrug.

11.2.2.2.16   Cranial Nerve Index

The cranial nerve index was significantly associated with group in Model 1 unadjusted and adjusted analyses of all participants (Table 11-20(a,b): Unadjusted RR=1.43, p=0.025; Adjusted RR=1.47, p=0.020). Of the Ranch Hands, 10.7 percent had an abnormal cranial nerve index, compared to 7.7 percent of Comparisons. After stratifying for military occupation, no significant associations between group and cranial nerve index were seen in unadjusted or adjusted analyses (Table 11-20(a,b): p>0.08 for all analyses).

No significant association between initial dioxin levels and the cranial nerve index was seen in the Model 2 unadjusted and adjusted analyses (Table 11-20(c,d): p>0.21 for both analyses).

In the Model 3 unadjusted analyses, significant relations were seen in the background dioxin category (Table 11-20(e): Unadjusted RR=1.61, p=0.019) and the low dioxin category (Table 11-20(e): Unadjusted RR=1.69, p=0.027).   These results remained significant after adjusting for covariates (Table 11-20(f): Adjusted RR=1.65, p=0.018 for background category; Adjusted RR=1.62, p=0.049 for low dioxin category). An abnormal cranial nerve index was observed for 11.5 percent of Ranch Hands in the background dioxin category and 12.4 percent of Ranch Hands in the low dioxin category, compared to 7.7 percent of Comparisons.

No significant associations were seen between cranial nerve index and 1987 dioxin levels in the Model 4 unadjusted and adjusted analyses (Table 11-20(g,h): p>0.32 for both analyses).

Table 11-20. Analysis of Cranial Nerve Index

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*82 (10.7)*	*1.43 (1.05,1.97)*	*0.025**
	Comparison	*1,157*	*89 (7.7)*		
Officer	Ranch Hand	303	35 (11.6)	1.54 (0.94,2.51)	0.085
	Comparison	460	36 (7.8)		
Enlisted Flyer	Ranch Hand	133	15 (11.3)	1.32 (0.63,2.77)	0.465
	Comparison	182	16 (8.8)		
Enlisted Groundcrew	Ranch Hand	332	32 (9.6)	1.38 (0.84,2.26)	0.204
	Comparison	515	37 (7.2)		

*: Statistically significant (0.010<p-value≤0.050).

Table 11-20. Analysis of Cranial Nerve Index (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,916*	*1.47 (1.06,2.04)*	*0.020**
Officer	763	1.54 (0.93,2.53)	0.091
Enlisted Flyer	312	1.31 (0.61,2.82)	0.487
Enlisted Groundcrew	841	1.49 (0.89,2.47)	0.128

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	19 (13.6)	0.85 (0.66,1.10)	0.214
Medium	141	11 (7.8)		
High	138	12 (8.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	0.99 (0.73,1.33)	0.926

[a]Relative risk for a twofold increase in initial dioxin.

Table 11-20. Analysis of Cranial Nerve Index (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,157	89 (7.7)		
Background RH	348	40 (11.5)	1.61 (1.08,2.39)	0.019*
Low RH	209	26 (12.4)	1.69 (1.06,2.69)	0.027*
High RH	210	16 (7.6)	0.96 (0.55,1.68)	0.895
Low plus High RH	419	42 (10.0)	1.28 (0.86,1.89)	0.226

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,152		
Background RH	347	1.65 (1.09,2.50)	0.018*
Low RH	208	1.62 (1.00,2.61)	0.049*
High RH	208	1.05 (0.59,1.89)	0.862
Low plus High RH	416	1.31 (0.87,1.97)	0.204

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-20. Analysis of Cranial Nerve Index (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	33 (12.7)	0.93 (0.81,1.08)	0.326
Medium	254	27 (10.6)		
High	254	22 (8.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	0.95 (0.79,1.14)	0.611

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.3 Physical Examination Variables – Peripheral Nerve Status

11.2.2.3.1 Pinprick

No significant associations were seen between pinprick and group or initial dioxin in the Model 1 and Model 2 unadjusted and adjusted analyses (Table 11-21(a-d): $p>0.09$ for all analyses).

A significant association was seen in the unadjusted and adjusted Model 3 analyses between categorized dioxin and pinprick in the high dioxin category (Table 11-21(e,f): Unadjusted RR=1.76, p=0.020; Adjusted RR=1.71, p=0.050). Ranch Hands in the high dioxin category were more likely to have had an abnormal pinprick (15.3%) than Comparisons (8.9%).

The Model 4 unadjusted and adjusted analyses showed no relation between 1987 dioxin levels and pinprick (Table 11-21(g,h): $p>0.13$ for both analyses).

Table 11-21. Analysis of Pinprick

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*637*	*69 (10.8)*	*1.24 (0.89,1.72)*	*0.212*
	Comparison	*984*	*88 (8.9)*		
Officer	Ranch Hand	258	26 (10.1)	1.25 (0.73,2.16)	0.415
	Comparison	390	32 (8.2)		
Enlisted Flyer	Ranch Hand	102	14 (13.7)	1.07 (0.51,2.22)	0.865
	Comparison	154	20 (13.0)		
Enlisted Groundcrew	Ranch Hand	277	29 (10.5)	1.31 (0.78,2.19)	0.300
	Comparison	440	36 (8.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,615*	*1.24 (0.86,1.77)*	*0.245*
Officer	648	1.16 (0.66,2.06)	0.606
Enlisted Flyer	253	1.04 (0.47,2.29)	0.920
Enlisted Groundcrew	714	1.42 (0.82,2.46)	0.206

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	109	10 (9.2)	1.23 (0.96,1.58)	0.099
Medium	114	13 (11.4)		
High	110	17 (15.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
332	1.26 (0.92,1.73)	0.155

[a]Relative risk for a twofold increase in initial dioxin.

Table 11-21. Analysis of Pinprick (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	984	88	(8.9)		
Background RH	303	28	(9.2)	1.11 (0.71,1.75)	0.640
Low RH	163	14	(8.6)	0.95 (0.53,1.71)	0.862
High RH	170	26	(15.3)	1.76 (1.09,2.82)	0.020*
Low plus High RH	333	40	(12.0)	1.30 (0.86,1.95)	0.208

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	980		
Background RH	302	1.19 (0.73,1.93)	0.482
Low RH	163	0.81 (0.43,1.52)	0.515
High RH	169	1.71 (1.00,2.93)	0.050*
Low plus High RH	332	1.19 (0.76,1.85)	0.450

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics				Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	228	20	(8.8)	1.13 (0.97,1.32)	0.131
Medium	206	20	(9.7)		
High	202	28	(13.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 11-21. Analysis of Pinprick (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
634	1.06 (0.86,1.30)	0.584

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.3.2   Light Touch

The unadjusted and adjusted Model 1 through Model 4 analyses showed no significant association between light touch and group or dioxin (Table 11-22(a-h): p>0.08 for all analyses).

Table 11-22. Analysis of Light Touch

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*637*	*40 (6.3)*	*1.11 (0.73,1.69)*	*0.625*
	Comparison	*984*	*56 (5.7)*		
Officer	Ranch Hand	258	16 (6.2)	1.45 (0.72,2.93)	0.299
	Comparison	390	17 (4.4)		
Enlisted Flyer	Ranch Hand	102	7 (6.9)	0.74 (0.29,1.89)	0.526
	Comparison	154	14 (9.1)		
Enlisted Groundcrew	Ranch Hand	277	17 (6.1)	1.09 (0.57,2.05)	0.800
	Comparison	440	25 (5.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,615*	*1.08 (0.69,1.69)*	*0.741*
Officer	648	1.34 (0.64,2.80)	0.430
Enlisted Flyer	253	0.68 (0.25,1.87)	0.460
Enlisted Groundcrew	714	1.11 (0.56,2.17)	0.768

Table 11-22. Analysis of Light Touch (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

	Initial Dioxin Category Summary Statistics		Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	109	7 (6.4)	1.22 (0.90,1.66)	0.204
Medium	114	8 (7.0)		
High	110	10 (9.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
332	1.32 (0.88,1.98)	0.174

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with an abnormal response to light touch.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	984	56 (5.7)		
Background RH	303	15 (5.0)	0.91 (0.50,1.64)	0.754
Low RH	163	9 (5.5)	0.96 (0.47,1.99)	0.919
High RH	170	16 (9.4)	1.66 (0.93,2.98)	0.088
Low plus High RH	333	25 (7.5)	1.27 (0.77,2.10)	0.346

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-22. Analysis of Light Touch (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	980		
Background RH	302	0.99 (0.53,1.85)	0.964
Low RH	163	0.86 (0.40,1.86)	0.709
High RH	169	1.42 (0.74,2.75)	0.291
Low plus High RH	332	1.11 (0.65,1.92)	0.696

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	228	12 (5.3)	1.17 (0.96,1.42)	0.129
Medium	206	12 (5.8)		
High	202	16 (7.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
634	1.11 (0.86,1.43)	0.414

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.3.3   Muscle Status

Neither group nor dioxin was significantly associated with muscle status in the Model 1 through Model 4 unadjusted and adjusted analyses (Table 11-23(a-h): p>0.51 for all analyses).

Table 11-23. Analysis of Muscle Status

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*43 (5.6)*	*1.14 (0.76,1.70)*	*0.541*
	Comparison	*1,168*	*58 (5.0)*		
Officer	Ranch Hand	303	17 (5.6)	1.25 (0.65,2.40)	0.512
	Comparison	461	21 (4.6)		
Enlisted Flyer	Ranch Hand	133	8 (6.0)	0.91 (0.36,2.30)	0.845
	Comparison	183	12 (6.6)		
Enlisted Groundcrew	Ranch Hand	332	18 (5.4)	1.14 (0.61,2.13)	0.671
	Comparison	524	25 (4.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,927*	*1.07 (0.70,1.63)*	*0.746*
Officer	764	1.12 (0.58,2.19)	0.737
Enlisted Flyer	313	0.87 (0.34,2.28)	0.784
Enlisted Groundcrew	850	1.13 (0.59,2.14)	0.716

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	10 (7.1)	1.03 (0.75,1.41)	0.854
Medium	143	7 (4.9)		
High	137	7 (5.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	1.06 (0.73,1.56)	0.751

[a]Relative risk for a twofold increase in initial dioxin.

Table 11-23. Analysis of Muscle Status (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,168	58 (5.0)		
Background RH	347	18 (5.2)	1.02 (0.59,1.77)	0.936
Low RH	211	12 (5.7)	1.16 (0.61,2.20)	0.648
High RH	209	12 (5.7)	1.19 (0.63,2.26)	0.598
Low plus High RH	420	24 (5.7)	1.17 (0.72,1.92)	0.520

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,163		
Background RH	346	1.00 (0.57,1.77)	0.989
Low RH	210	1.09 (0.56,2.11)	0.794
High RH	207	1.09 (0.55,2.16)	0.806
Low plus High RH	417	1.09 (0.65,1.82)	0.741

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	14 (5.5)	0.98 (0.81,1.20)	0.866
Medium	257	14 (5.4)		
High	254	14 (5.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 11-23. Analysis of Muscle Status (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
763	0.96 (0.76,1.20)	0.701

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.3.4   Patellar Reflex

When contrasting active and very active patellar reflexes to sluggish and absent patellar reflexes, no significant association was seen in the Model 1 through Model 4 unadjusted and adjusted analyses (Table 11-24(a-h): p>0.06 for all analyses).

When sluggish, active, and very active patellar reflexes were compared to the absence of a patellar reflex, no significant associations were seen in Model 1 or Model 2 unadjusted or adjusted analyses (Table 11-24(a-d): p>0.09 for all analyses). In Model 3 unadjusted analyses, however, a significant association was seen for Ranch Hands in the low and high dioxin categories combined (Table 11-24(e): Unadjusted RR=1.84, p=0.025). After adjusting for covariates, the results remained significant for the combined low and high dioxin category (Table 11-24(f): Adjusted RR=1.89, p=0.027) and were significant for the high dioxin category as well (Table 11-24(f): Adjusted RR=2.11, p=0.048). More Ranch Hands in the high dioxin category or in the low and high dioxin categories combined had an absent patellar reflex (5.7% for each category) than Comparisons (3.0%). The Model 4 unadjusted and adjusted analyses showed a significant association between 1987 dioxin levels and the patellar reflex (Table 11-24(g,h): Unadjusted RR=1.29, p=0.017; Adjusted RR=1.44, p=0.013). Of the Ranch Hands in the low 1987 dioxin category, 2.3 percent had an absent patellar reflex, compared to 5.5 percent of Ranch Hands in the medium 1987 dioxin category and 5.1 percent of Ranch Hands in the high 1987 dioxin category.

11.2.2.3.5   Achilles Reflex

When active and very active Achilles reflexes were contrasted with sluggish and absent reflexes, a significant association with exposure group was seen for officers in the Model 1 unadjusted and adjusted analyses (Table 11-25(a,b): Unadjusted RR=1.46, p=0.013; Adjusted RR=1.42, p=0.031). Ranch Hand officers were more likely to have sluggish or absent Achilles reflexes (66.0%) than Comparison officers (57.1%). No difference between Ranch Hands and Comparisons was seen in the unadjusted or adjusted Model 1 analyses for all participants or for enlisted flyers and groundcrew (Table 11-25(a,b): p>0.16 for all analyses). No significant associations for this contrast were seen in Model 2, Model 3, or Model 4 unadjusted and adjusted analyses (Table 11-25(c-h): p≥0.07 for all analyses).

When sluggish, active, and very active Achilles reflexes were compared to absent reflexes, no significant relations were with group or initial dioxin in the Model 1 and Model 2 unadjusted or adjusted analyses (Table 11-25(a-d): p>0.25 for all analyses). In the Model 3 unadjusted analyses, a significant association was seen in the low dioxin category (Table 11-25(e): Unadjusted RR=1.45, p=0.029). After adjusting for covariates, however, this association was no longer significant (Table 11-25(f): p=0.167). No other Model 3 or Model 4 unadjusted or adjusted contrast was significant (Table 11-25(e-h): p>0.13 for all analyses).

Table 11-24. Analysis of Patellar Reflex

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

| Occupational Category | Group | n | Number (%) | | | Sluggish or Absent vs. Very Active or Active | | Absent vs. Very Active, Active, or Sluggish | |
			Absent	Sluggish	Active or Very Active	Unadjusted Relative Risk (95% C.I.)	p-Value	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*33 (4.3)*	*163 (21.2)*	*574 (74.6)*	*0.94 (0.77,1.16)*	*0.592*	*1.44 (0.89,2.34)*	*0.139*
	Comparison	*1,164*	*35 (3.0)*	*274 (23.5)*	*855 (73.5)*				
Officer	Ranch Hand	306	15 (4.9)	62 (20.3)	229 (74.8)	0.85 (0.61,1.18)	0.327	1.52 (0.73,3.16)	0.260
	Comparison	458	15 (3.3)	115 (25.1)	328 (71.6)				
Enlisted Flyer	Ranch Hand	133	4 (3.0)	31 (23.3)	98 (73.7)	0.90 (0.54,1.49)	0.680	1.10 (0.29,4.19)	0.885
	Comparison	183	5 (2.7)	47 (25.7)	131 (71.6)				
Enlisted Groundcrew	Ranch Hand	331	14 (4.2)	70 (21.2)	247 (74.6)	1.06 (0.77,1.46)	0.718	1.50 (0.71,3.14)	0.287
	Comparison	523	15 (2.9)	112 (21.4)	396 (75.7)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

| Occupational Category | n | Sluggish or Absent vs. Very Active or Active | | Absent vs. Very Active, Active, or Sluggish | |
		Adjusted Relative Risk (95% C.I.)	p-Value	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,926*	*0.94 (0.76,1.18)*	*0.608*	*1.48 (0.89,2.44)*	*0.130*
Officer	764	0.83 (0.59,1.17)	0.283	1.48 (0.70,3.13)	0.307
Enlisted Flyer	313	0.85 (0.50,1.44)	0.543	1.11 (0.28,4.30)	0.885
Enlisted Groundcrew	849	1.12 (0.80,1.56)	0.512	1.61 (0.75,3.45)	0.217

Table 11-24. Analysis of Patellar Reflex (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

| | | Initial Dioxin Category Summary Statistics | | | Analysis Results for Log$_2$ (Initial Dioxin)[a] | | | | |
| | | | Number (%) | | Sluggish or Absent vs. Very Active or Active | | Absent vs. Very Active, Active, or Sluggish | | |
Initial Dioxin Category	n	Absent	Sluggish	Active or Very Active	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]	p-Value
Low	139	9 (6.5)	35 (25.2)	95 (68.4)	0.96 (0.82,1.13)	0.630	1.17 (0.87,1.56)	0.305
Medium	143	5 (3.5)	35 (24.5)	103 (72.0)				
High	138	10 (7.3)	29 (21.0)	99 (71.7)				

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (Initial Dioxin) | | | | |
| | Sluggish or Absent vs. Very Active or Active | | Absent vs. Very Active, Active, or Sluggish | |
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	1.02 (0.83,1.25)	0.873	1.37 (0.95,1.99)	0.093

[a]Relative risk for a twofold increase in initial dioxin.

Table 11-24. Analysis of Patellar Reflex (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Absent	Number (%) Sluggish	Number (%) Active or Very Active	Sluggish or Absent vs. Very Active or Active Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Absent vs. Very Active, Active, or Sluggish Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,164	35 (3.0)	274 (23.5)	855 (73.5)				
Background RH	349	9 (2.6)	64 (18.3)	276 (79.1)	0.80 (0.60,1.08)	0.144	0.94 (0.44,1.98)	0.867
Low RH	210	12 (5.7)	53 (25.2)	145 (69.1)	1.21 (0.88,1.67)	0.248	1.89 (0.96,3.72)	0.064
High RH	210	12 (5.7)	46 (21.9)	152 (72.4)	0.97 (0.69,1.35)	0.855	1.80 (0.91,3.54)	0.090
Low plus High RH	420	24 (5.7)	99 (23.6)	297 (70.7)	1.08 (0.84,1.39)	0.532	1.84 (1.08,3.15)	0.025*

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Sluggish or Absent vs. Very Active or Active Adjusted Relative Risk (95% C.I.)[a]	p-Value	Absent vs. Very Active, Active, or Sluggish Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,160				
Background RH	348	0.81 (0.59,1.09)	0.165	0.94 (0.43,2.03)	0.866
Low RH	209	1.10 (0.79,1.55)	0.564	1.69 (0.84,3.41)	0.140
High RH	208	1.02 (0.71,1.47)	0.895	2.11 (1.01,4.43)	0.048*
Low plus High RH	417	1.06 (0.82,1.39)	0.648	1.89 (1.07,3.33)	0.027*

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-24. Analysis of Patellar Reflex (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

		1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)[a]			
					Sluggish or Absent vs. Very Active or Active		Absent vs. Very Active, Active, or Sluggish	
			Number (%)					
1987 Dioxin Category	n	Absent	Sluggish	Active or Very Active	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	258	6 (2.3)	43 (16.7)	209 (81.0)	1.10 (0.99,1.21)	0.069	1.29 (1.05,1.59)	0.017*
Medium	256	14 (5.5)	62 (24.2)	180 (70.3)				
High	255	13 (5.1)	58 (22.8)	184 (72.2)				

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log_2 (1987 Dioxin) | | | |
| | Sluggish or Absent vs. Very Active or Active | | Absent vs. Very Active, Active, or Sluggish | |
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
765	1.04 (0.92,1.19)	0.526	1.44 (1.07,1.95)	0.013*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Table 11-25. Analysis of Achilles Reflex

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%)			Sluggish or Absent vs. Very Active or Active		Absent vs. Very Active, Active, or Sluggish	
			Absent	Sluggish	Active or Very Active	Unadjusted Relative Risk (95% C.I.)	p-Value	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*186 (24.1)*	*277 (35.9)*	*309 (40.0)*	*1.14 (0.95,1.37)*	*0.169*	*1.13 (0.91,1.41)*	*0.258*
	Comparison	*1,165*	*255 (21.9)*	*407 (34.9)*	*503 (43.2)*				
Officer	Ranch Hand	306	81 (26.5)	121 (39.5)	104 (34.0)	1.46 (1.08,1.97)	0.013*	1.17 (0.84,1.63)	0.356
	Comparison	459	108 (23.5)	154 (33.6)	197 (42.9)				
Enlisted Flyer	Ranch Hand	133	37 (27.8)	47 (35.3)	49 (36.8)	0.93 (0.58,1.48)	0.759	1.08 (0.65,1.78)	0.775
	Comparison	182	48 (26.4)	70 (38.5)	64 (35.2)				
Enlisted Groundcrew	Ranch Hand	333	68 (20.4)	109 (32.7)	156 (46.9)	0.97 (0.74,1.28)	0.849	1.10 (0.78,1.55)	0.582
	Comparison	524	99 (18.9)	183 (34.9)	242 (46.2)				

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Sluggish or Absent vs. Very Active or Active		Absent vs. Very Active, Active, or Sluggish	
		Adjusted Relative Risk (95% C.I.)	p-Value	Adjusted Relative Risk (95% C.I.)	p-Value
All	1,928	*1.10 (0.90,1.34)*	*0.357*	*1.13 (0.89,1.43)*	*0.321*
Officer	765	1.42 (1.03,1.95)	0.031*	1.14 (0.79,1.63)	0.478
Enlisted Flyer	312	0.89 (0.55,1.46)	0.646	1.03 (0.60,1.76)	0.928
Enlisted Groundcrew	851	0.95 (0.70,1.27)	0.709	1.17 (0.80,1.70)	0.422

*: Statistically significant (0.010<p-value≤0.050).

Table 11-25. Analysis of Achilles Reflex (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

		Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]				
					Sluggish or Absent vs. Very Active or Active		Absent vs. Very Active, Active, or Sluggish		
			Number (%)						
Initial Dioxin Category	n	Absent	Sluggish	Active or Very Active	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	
Low	140	46 (32.9)	45 (32.1)	49 (35.0)	0.88 (0.76,1.03)	0.107	0.93 (0.79,1.10)	0.394	
Medium	143	31 (21.7)	56 (39.2)	56 (39.2)					
High	138	36 (26.1)	43 (31.2)	59 (42.8)					

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

| | Analysis Results for Log_2 (Initial Dioxin) | | | | |
| | Sluggish or Absent vs. Very Active or Active | | Absent vs. Very Active, Active, or Sluggish | | |
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value	
418	1.05 (0.86,1.28)	0.656	1.04 (0.84,1.30)	0.704	

[a]Relative risk for a twofold increase in initial dioxin.

Table 11-25. Analysis of Achilles Reflex (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Absent	Number (%) Sluggish	Number (%) Active or Very Active	Sluggish or Absent vs. Very Active or Active Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Absent vs. Very Active, Active, or Sluggish Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,165	255 (21.9)	407 (34.9)	503 (43.2)				
Background RH	350	73 (20.9)	133 (38.0)	144 (41.1)	1.20 (0.94,1.53)	0.149	1.07 (0.79,1.44)	0.669
Low RH	211	62 (29.4)	73 (34.6)	76 (36.0)	1.33 (0.98,1.81)	0.070	1.45 (1.04,2.02)	0.029*
High RH	210	51 (24.3)	71 (33.8)	88 (41.9)	0.97 (0.72,1.31)	0.842	1.03 (0.72,1.46)	0.872
Low plus High RH	421	113 (26.8)	144 (34.2)	164 (39.0)	1.14 (0.90,1.43)	0.281	1.22 (0.94,1.59)	0.133

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Sluggish or Absent vs. Very Active or Active Adjusted Relative Risk (95% C.I.)[a]	p-Value	Absent vs. Very Active, Active, or Sluggish Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,160				
Background RH	349	1.13 (0.87,1.47)	0.370	1.04 (0.75,1.44)	0.810
Low RH	210	1.13 (0.82,1.57)	0.463	1.29 (0.90,1.85)	0.167
High RH	208	1.05 (0.75,1.46)	0.794	1.15 (0.77,1.72)	0.490
Low plus High RH	418	1.09 (0.85,1.40)	0.511	1.22 (0.91,1.63)	0.181

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-25. Analysis of Achilles Reflex (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics					Analysis Results for Log_2 (1987 Dioxin)[a]			
		Number (%)			Sluggish or Absent vs. Very Active or Active		Absent vs. Very Active, Active, or Sluggish	
1987 Dioxin Category	n	Absent	Sluggish	Active or Very Active	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	258	53 (20.5)	100 (38.8)	105 (40.7)	0.98 (0.90,1.07)	0.652	1.05 (0.95,1.17)	0.321
Medium	258	72 (27.9)	88 (34.1)	98 (38.0)				
High	255	61 (23.9)	89 (34.9)	105 (41.2)				

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)			
	Sluggish or Absent vs. Very Active or Active		Absent vs. Very Active, Active, or Sluggish	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
767	0.98 (0.87,1.10)	0.738	1.03 (0.90,1.18)	0.671

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.3.6   Biceps Reflex

No significant association was seen between group or dioxin and the biceps reflex in the Model 1 through Model 4 unadjusted and adjusted analyses, either when absent and sluggish reflexes were compared to active and very active reflexes (Table 11-26(a-h): p>0.05 for all contrasts), or when absent reflexes were compared to sluggish, active, and very active reflexes (Table 11-26(a-h): p>0.08 for all contrasts).

11.2.2.3.7   Babinski Reflex

The Babinski reflex was not significantly associated with group or dioxin in the Model 1 through Model 4 unadjusted and adjusted analyses (Table 11-27(a-h): p>0.24 for all analyses).

11.2.2.3.8   Any Symmetric Peripheral Abnormality

No significant associations were seen between any symmetrical peripheral abnormality and group or initial dioxin level in the Model 1 and Model 2 unadjusted and adjusted analyses (Table 11-28(a-d): p>0.18 for all analyses).

In the Model 3 unadjusted analyses, a significant association was seen in the low dioxin category (Table 11-28(e): Unadjusted RR=1.46, p=0.027). After adjusting for covariates, however, the relation was no longer significant (Table 11-28(f): p=0.244). No other unadjusted or adjusted Model 3 contrast was significant (Table 11-28(e,f): p>0.05 for all contrasts).

Model 4 unadjusted and adjusted analyses showed no significant relation between 1987 dioxin levels and any symmetrical peripheral abnormality (Table 11-28(g,h): p>0.24 for all analyses).

11.2.2.3.9   Possible Peripheral Neuropathy

No significant associations were seen in the Model 1 and Model 2 unadjusted and adjusted analyses of possible peripheral neuropathy (Table 11-29(a-d): p>0.32 for all analyses).

A significant association in the Model 3 unadjusted analyses was seen in the low dioxin category (Table 11-29(e): Unadjusted RR=1.45, p=0.034), but no significant associations were seen in the other dioxin categories (Table 11-29(e): p≥0.12 for all analyses). No significant associations were seen in the Model 3 analyses after adjusting for covariates (Table 11-29(f): p>0.26 for all contrasts).

The Model 4 unadjusted and adjusted analyses showed no significant relation between possible peripheral neuropathy and 1987 dioxin levels (Table 11-29(g,h): p>0.25 for all analyses).

11.2.2.3.10   Probable Peripheral Neuropathy

Probable peripheral neuropathy was not significantly associated with group or dioxin in the Model 1 through Model 4 unadjusted and adjusted analyses (Table 11-30(a-h): p>0.15 for all analyses).

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Table 11-26. Analysis of Biceps Reflex

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%)			Sluggish or Absent vs. Very Active or Active		Absent vs. Very Active, Active, or Sluggish	
			Absent	Sluggish	Active or Very Active	Unadjusted Relative Risk (95% C.I.)	p-Value	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*18 (2.3)*	*209 (27.0)*	*546 (70.6)*	*0.99 (0.81,1.21)*	*0.935*	*1.14 (0.61,2.11)*	*0.686*
	Comparison	*1,168*	*24 (2.1)*	*321 (27.5)*	*823 (70.5)*				
Officer	Ranch Hand	306	3 (1.0)	85 (27.8)	218 (71.2)	0.96 (0.70,1.33)	0.825	0.41 (0.11,1.46)	0.168
	Comparison	461	11 (2.4)	125 (27.1)	325 (70.5)				
Enlisted Flyer	Ranch Hand	133	6 (4.5)	32 (24.1)	95 (71.4)	0.76 (0.47,1.24)	0.271	1.39 (0.44,4.42)	0.573
	Comparison	183	6 (3.3)	57 (31.2)	120 (65.6)				
Enlisted Groundcrew	Ranch Hand	334	9 (2.7)	92 (27.5)	233 (69.8)	1.12 (0.83,1.52)	0.453	2.05 (0.75,5.55)	0.160
	Comparison	524	7 (1.3)	139 (26.5)	378 (72.1)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Sluggish or Absent vs. Very Active or Active		Absent vs. Very Active, Active, or Sluggish	
		Adjusted Relative Risk (95% C.I.)	p-Value	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,932*	*1.02 (0.82,1.25)*	*0.877*	*1.08 (0.57,2.04)*	*0.825*
Officer	767	0.97 (0.70,1.34)	0.842	0.38 (0.10,1.41)	0.148
Enlisted Flyer	313	0.73 (0.44,1.21)	0.220	1.24 (0.38,4.05)	0.724
Enlisted Groundcrew	852	1.21 (0.89,1.66)	0.228	2.11 (0.76,5.81)	0.150

Table 11-26. Analysis of Biceps Reflex (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

| | | Initial Dioxin Category Summary Statistics | | | Analysis Results for Log_2 (Initial Dioxin)[a] | | | |
| | | | Number (%) | | Sluggish or Absent vs. Very Active or Active | | Absent vs. Very Active, Active, or Sluggish | |
Initial Dioxin Category	n	Absent	Sluggish	Active or Very Active	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]	p-Value
Low	140	3 (2.1)	49 (35.0)	88 (62.9)	0.92 (0.78,1.07)	0.264	1.38 (0.94,2.02)	0.107
Medium	143	4 (2.8)	44 (30.8)	95 (66.4)				
High	138	6 (4.4)	34 (24.6)	98 (71.0)				

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

| | Analysis Results for Log_2 (Initial Dioxin) | | | |
| | Sluggish or Absent vs. Very Active or Active | | Absent vs. Very Active, Active, or Sluggish | |
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	0.92 (0.75,1.12)	0.410	1.40 (0.85,2.30)	0.181

[a]Relative risk for a twofold increase in initial dioxin.

Table 11-26. Analysis of Biceps Reflex (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Absent	Number (%) Sluggish	Number (%) Active or Very Active	Sluggish or Absent vs. Very Active or Active Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Absent vs. Very Active, Active, or Sluggish Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,168	24 (2.1)	321 (27.5)	823 (70.5)				
Background RH	351	5 (1.4)	82 (23.4)	264 (75.2)	0.84 (0.64,1.11)	0.231	0.73 (0.28,1.95)	0.535
Low RH	211	5 (2.4)	72 (34.1)	134 (63.5)	1.35 (0.99,1.84)	0.058	1.13 (0.43,3.01)	0.803
High RH	210	8 (3.8)	55 (26.2)	147 (70.0)	0.96 (0.69,1.33)	0.801	1.79 (0.79,4.05)	0.166
Low plus High RH	421	13 (3.1)	127 (30.2)	281 (66.8)	1.14 (0.89,1.45)	0.294	1.42 (0.71,2.86)	0.325

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Sluggish or Absent vs. Very Active or Active Adjusted Relative Risk (95% C.I.)[a]	p-Value	Absent vs. Very Active, Active, or Sluggish Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,163				
Background RH	350	0.88 (0.66,1.18)	0.397	0.75 (0.27,2.04)	0.569
Low RH	210	1.29 (0.94,1.78)	0.118	0.97 (0.35,2.64)	0.947
High RH	208	0.99 (0.70,1.40)	0.944	1.67 (0.69,4.04)	0.258
Low plus High RH	418	1.13 (0.88,1.46)	0.345	1.27 (0.61,2.64)	0.526

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-26. Analysis of Biceps Reflex (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

| 1987 Dioxin Category Summary Statistics | | | | | Analysis Results for Log$_2$ (1987 Dioxin)[a] | | | | |
| | | | Number (%) | | Sluggish or Absent vs. Very Active or Active | | Absent vs. Very Active, Active, or Sluggish | | |
1987 Dioxin Category	n	Absent	Sluggish	Active or Very Active	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	4 (1.5)	55 (21.2)	200 (77.2)	1.08 (0.98,1.19)	0.102	1.28 (0.97,1.69)	0.082
Medium	258	4 (1.6)	87 (33.7)	167 (64.7)				
High	255	10 (3.9)	67 (26.3)	178 (69.8)				

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (1987 Dioxin) | | | | |
| | Sluggish or Absent vs. Very Active or Active | | Absent vs. Very Active, Active, or Sluggish | | |
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	1.06 (0.94,1.20)	0.332	1.19 (0.85,1.68)	0.302

[a]Relative risk for a twofold increase in 1987 dioxin.

Table 11-27. Analysis of Babinski Reflex

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*10 (1.3)*	*0.84 (0.38,1.82)*	*0.650*
	Comparison	*1,165*	*18 (1.5)*		
Officer	Ranch Hand	306	3 (1.0)	1.13 (0.25,5.07)	0.877
	Comparison	459	4 (0.9)		
Enlisted Flyer	Ranch Hand	133	4 (3.0)	1.39 (0.34,5.65)	0.648
	Comparison	183	4 (2.2)		
Enlisted Groundcrew	Ranch Hand	333	3 (0.9)	0.47 (0.13,1.71)	0.249
	Comparison	523	10 (1.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,928*	*0.82 (0.37,1.83)*	*0.634*
Officer	765	1.16 (0.25,5.29)	0.851
Enlisted Flyer	313	1.32 (0.32,5.52)	0.700
Enlisted Groundcrew	850	0.47 (0.13,1.75)	0.260

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	2 (1.4)	0.86 (0.42,1.73)	0.655
Medium	143	2 (1.4)		
High	138	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	1.48 (0.51,4.32)	0.481

[a]Relative risk for a twofold increase in initial dioxin.

Table 11-27. Analysis of Babinski Reflex (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,165	18 (1.5)		
Background RH	350	5 (1.4)	1.07 (0.39,2.93)	0.893
Low RH	211	3 (1.4)	0.86 (0.25,2.96)	0.806
High RH	210	2 (1.0)	0.53 (0.12,2.33)	0.401
Low plus High RH	421	5 (1.2)	0.67 (0.24,1.87)	0.450

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,160		
Background RH	349	1.27 (0.45,3.61)	0.652
Low RH	210	0.82 (0.23,2.91)	0.761
High RH	208	0.44 (0.10,2.01)	0.292
Low plus High RH	418	0.60 (0.21,1.72)	0.345

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	3 (1.2)	0.83 (0.56,1.25)	0.373
Medium	257	4 (1.6)		
High	255	3 (1.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 11-27. Analysis of Babinski Reflex (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
767	0.79 (0.52,1.20)	0.277

[a]Relative risk for a twofold increase in 1987 dioxin.

Table 11-28. Analysis of Any Symmetric Peripheral Abnormality

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*750*	*185 (24.7)*	*1.16 (0.93,1.44)*	*0.186*
	Comparison	*1,130*	*249 (22.0)*		
Officer	Ranch Hand	298	77 (25.8)	1.19 (0.84,1.67)	0.326
	Comparison	445	101 (22.7)		
Enlisted Flyer	Ranch Hand	130	39 (30.0)	1.29 (0.77,2.13)	0.331
	Comparison	176	44 (25.0)		
Enlisted Groundcrew	Ranch Hand	322	69 (21.4)	1.06 (0.75,1.50)	0.730
	Comparison	509	104 (20.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,863*	*1.14 (0.90,1.45)*	*0.288*
Officer	740	1.19 (0.82,1.73)	0.357
Enlisted Flyer	302	1.18 (0.68,2.05)	0.560
Enlisted Groundcrew	821	1.07 (0.73,1.57)	0.716

Table 11-28.   Analysis of Any Symmetric Peripheral Abnormality (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Present**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	140	46 (32.9)	0.94 (0.79,1.11)	0.436
Medium	138	34 (24.6)		
High	134	36 (26.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
407	1.06 (0.85,1.31)	0.610

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,130	249 (22.0)		
Background RH	337	68 (20.2)	1.03 (0.76,1.41)	0.834
Low RH	209	62 (29.7)	1.46 (1.04,2.04)	0.027*
High RH	203	54 (26.6)	1.14 (0.80,1.61)	0.478
Low plus High RH	412	116 (28.2)	1.29 (0.99,1.68)	0.058

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,120		
Background RH	335	1.02 (0.73,1.42)	0.917
Low RH	206	1.25 (0.86,1.80)	0.244
High RH	201	1.24 (0.83,1.84)	0.295
Low plus High RH	407	1.24 (0.93,1.66)	0.148

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	252	53 (21.0)	1.06 (0.96,1.18)	0.246
Medium	251	66 (26.3)		
High	246	65 (26.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
742	1.03 (0.90,1.18)	0.675

[a]Relative risk for a twofold increase in 1987 dioxin.

Table 11-29. Analysis of Possible Peripheral Neuropathy

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*750*	*175 (23.3)*	*1.12 (0.90,1.39)*	*0.323*
	Comparison	*1,131*	*242 (21.4)*		
Officer	Ranch Hand	298	72 (24.2)	1.11 (0.79,1.57)	0.544
	Comparison	445	99 (22.2)		
Enlisted Flyer	Ranch Hand	130	37 (28.5)	1.28 (0.76,2.14)	0.349
	Comparison	177	42 (23.7)		
Enlisted Groundcrew	Ranch Hand	322	66 (20.5)	1.04 (0.74,1.47)	0.819
	Comparison	509	101 (19.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,864*	*1.10 (0.86,1.41)*	*0.443*
Officer	740	1.11 (0.76,1.63)	0.585
Enlisted Flyer	303	1.16 (0.66,2.04)	0.602
Enlisted Groundcrew	821	1.06 (0.72,1.57)	0.754

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	44 (31.4)	0.92 (0.77,1.09)	0.327
Medium	138	33 (23.9)		
High	134	33 (24.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
407	1.01 (0.81,1.26)	0.915

[a]Relative risk for a twofold increase in initial dioxin.

Table 11-29. Analysis of Possible Peripheral Neuropathy (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,131	242 (21.4)		
Background RH	337	64 (19.0)	1.00 (0.73,1.37)	0.990
Low RH	209	60 (28.7)	1.45 (1.03,2.03)	0.034*
High RH	203	50 (24.6)	1.05 (0.73,1.51)	0.780
Low plus High RH	412	110 (26.7)	1.24 (0.95,1.62)	0.120

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,121		
Background RH	335	1.00 (0.71,1.40)	0.981
Low RH	206	1.24 (0.85,1.80)	0.269
High RH	201	1.14 (0.76,1.71)	0.539
Low plus High RH	407	1.19 (0.88,1.60)	0.263

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	252	49 (19.4)	1.06 (0.96,1.18)	0.254
Medium	251	64 (25.5)		
High	246	61 (24.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 11-29. Analysis of Possible Peripheral Neuropathy (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
742	1.01 (0.88,1.17)	0.851

[a]Relative risk for a twofold increase in 1987 dioxin.

Table 11-30. Analysis of Probable Peripheral Neuropathy

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*749*	*62 (8.3)*	*1.20 (0.85,1.70)*	*0.300*
	Comparison	*1,131*	*79 (7.0)*		
Officer	Ranch Hand	298	31 (10.4)	1.45 (0.87,2.42)	0.157
	Comparison	445	33 (7.4)		
Enlisted Flyer	Ranch Hand	130	14 (10.8)	1.41 (0.65,3.06)	0.392
	Comparison	177	14 (7.9)		
Enlisted Groundcrew	Ranch Hand	321	17 (5.3)	0.83 (0.45,1.53)	0.556
	Comparison	509	32 (6.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,863*	*1.19 (0.81,1.75)*	*0.380*
Officer	740	1.47 (0.84,2.57)	0.179
Enlisted Flyer	303	1.33 (0.56,3.14)	0.522
Enlisted Groundcrew	820	0.84 (0.43,1.63)	0.597

Table 11-30. Analysis of Probable Peripheral Neuropathy (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Present**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	140	13 (9.3)	1.01 (0.79,1.30)	0.920
Medium	138	12 (8.7)		
High	133	12 (9.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
406	1.26 (0.88,1.81)	0.198

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,131	79 (7.0)		
Background RH	337	25 (7.4)	1.24 (0.77,1.99)	0.376
Low RH	209	18 (8.6)	1.19 (0.69,2.05)	0.525
High RH	202	19 (9.4)	1.22 (0.71,2.08)	0.468
Low plus High RH	411	37 (9.0)	1.21 (0.80,1.83)	0.378

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 11-30. Analysis of Probable Peripheral Neuropathy (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,121		
Background RH	335	1.29 (0.77,2.18)	0.330
Low RH	206	0.93 (0.51,1.68)	0.805
High RH	200	1.40 (0.75,2.62)	0.290
Low plus High RH	406	1.14 (0.71,1.81)	0.590

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	252	17 (6.7)	1.05 (0.89,1.23)	0.550
Medium	251	22 (8.8)		
High	245	23 (9.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
741	0.96 (0.75,1.22)	0.725

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.4 Physical Examination Variables – CNS Coordination Processes

11.2.2.4.1   Tremor

No significant association was seen between tremors and group or dioxin in the Model 1 through Model 4 unadjusted and adjusted analyses (Table 11-31(a-h): p>0.14 for all analyses).

Table 11-31. Analysis of Tremor

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*54 (7.0)*	*0.95 (0.66,1.35)*	*0.757*
	Comparison	*1,169*	*86 (7.4)*		
Officer	Ranch Hand	306	20 (6.5)	0.94 (0.53,1.67)	0.827
	Comparison	461	32 (6.9)		
Enlisted Flyer	Ranch Hand	133	10 (7.5)	0.98 (0.42,2.28)	0.965
	Comparison	183	14 (7.7)		
Enlisted Groundcrew	Ranch Hand	334	24 (7.2)	0.94 (0.55,1.59)	0.814
	Comparison	525	40 (7.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,933*	*0.93 (0.65,1.34)*	*0.705*
Officer	767	0.89 (0.50,1.60)	0.700
Enlisted Flyer	313	0.97 (0.41,2.28)	0.950
Enlisted Groundcrew	853	0.95 (0.56,1.63)	0.861

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	7 (5.0)	1.20 (0.92,1.56)	0.192
Medium	143	12 (8.4)		
High	138	11 (8.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	1.28 (0.91,1.82)	0.160

[a]Relative risk for a twofold increase in initial dioxin.

Table 11-31. Analysis of Tremor (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,169	86 (7.4)		
Background RH	351	24 (6.8)	0.94 (0.59,1.51)	0.795
Low RH	211	10 (4.7)	0.62 (0.32,1.22)	0.168
High RH	210	20 (9.5)	1.31 (0.78,2.18)	0.306
Low plus High RH	421	30 (7.1)	0.90 (0.57,1.42)	0.654

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,164		
Background RH	350	0.94 (0.58,1.52)	0.790
Low RH	210	0.60 (0.30,1.19)	0.142
High RH	208	1.30 (0.75,2.24)	0.345
Low plus High RH	418	0.88 (0.55,1.40)	0.594

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	18 (6.9)	1.09 (0.92,1.29)	0.318
Medium	258	14 (5.4)		
High	255	22 (8.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 11-31. Analysis of Tremor (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
768	1.03 (0.83,1.27)	0.798

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.4.2   Coordination

As a reminder, coordination was a composite index defined as "normal" if the Romberg sign, finger-nose-finger and heel-knee-shin coordination processes, rapidly alternating movements of pronation and supination of hands, and rapid patting were normal, and abnormal otherwise.

No difference in coordination was seen between Ranch Hands and Comparisons in the Model 1 unadjusted and adjusted analyses (Table 11-32(a,b): p>0.20 for all analyses).

No relation between coordination and initial dioxin was seen in the unadjusted Model 2 analysis (Table 11-32(c): p=0.148). This relation, however, was significant after adjusting for covariates (Table 11-32(d): Adjusted RR=2.25, p=0.002). Ranch Hands in the high dioxin category were more likely to have abnormal coordination (5.8%), followed by Ranch Hands in the low category (2.9%), then Ranch Hands in the medium category (2.1%). The difference between the unadjusted and adjusted results was partially due to more Romberg sign abnormalities in officers than enlisted personnel, for Ranch Hands with an initial dioxin estimate.

No significant associations were seen between coordination and categorized dioxin or 1987 dioxin levels in the Model 3 and Model 4 unadjusted and adjusted analyses (Table 11-32(e-h): p>0.08 for all analyses).

Table 11-32. Analysis of Coordination

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*31 (4.0)*	*0.76 (0.49,1.18)*	*0.221*
	Comparison	*1,168*	*61 (5.2)*		
Officer	Ranch Hand	306	13 (4.2)	1.03 (0.50,2.12)	0.931
	Comparison	461	19 (4.1)		
Enlisted Flyer	Ranch Hand	132	6 (4.5)	0.62 (0.23,1.68)	0.351
	Comparison	183	13 (7.1)		
Enlisted Groundcrew	Ranch Hand	332	12 (3.6)	0.64 (0.32,1.27)	0.203
	Comparison	524	29 (5.5)		

Table 11-32. Analysis of Coordination (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*0.75 (0.47,1.19)*	*0.218*
Officer	767	0.99 (0.47,2.07)	0.971
Enlisted Flyer	312	0.63 (0.22,1.76)	0.373
Enlisted Groundcrew	851	0.64 (0.31,1.31)	0.223

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	4 (2.9)	1.31 (0.92,1.88)	0.148
Medium	141	3 (2.1)		
High	138	8 (5.8)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	2.25 (1.30,3.90)	0.002**

[a]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Table 11-32. Analysis of Coordination (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,168	61 (5.2)		
Background RH	350	16 (4.6)	0.88 (0.50,1.55)	0.650
Low RH	210	6 (2.9)	0.53 (0.23,1.25)	0.147
High RH	209	9 (4.3)	0.81 (0.40,1.66)	0.567
Low plus High RH	419	15 (3.6)	0.66 (0.37,1.18)	0.160

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,163		
Background RH	349	0.93 (0.51,1.70)	0.823
Low RH	210	0.46 (0.19,1.11)	0.083
High RH	207	0.80 (0.37,1.71)	0.559
Low plus High RH	417	0.60 (0.33,1.12)	0.109

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	12 (4.6)	1.00 (0.80,1.25)	0.989
Medium	257	8 (3.1)		
High	253	11 (4.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 11-32. Analysis of Coordination (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
766	1.06 (0.79,1.41)	0.719

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.4.3 Romberg Sign

No significant associations were seen between the Romberg sign and group in the Model 1 unadjusted and adjusted analyses (Table 11-33(a,b): p>0.25 for all analyses).

The unadjusted analysis of Model 2 showed no association between initial dioxin and the Romberg sign (Table 11-33(c): p=0.961). After adjusting for covariates, however, the association was significant (Table 11-33(d): Adjusted RR=2.11, p=0.033). The difference between the unadjusted and adjusted results was partially due to more Romberg sign abnormalities in officers than enlisted personnel, for Ranch Hands with an initial dioxin estimate. One more Ranch Hand in the low initial dioxin category and the high initial dioxin categories had an abnormal Romberg sign (2.9% for each category) than in the medium category (2.1%).

The associations between Romberg sign and dioxin in Models 3 and 4 unadjusted and adjusted analyses were nonsignificant (Table 11-33(e-h): p>0.12 for all analyses).

Table 11-33. Analysis of Romberg Sign

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Abnormal**	**Unadjusted Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*772*	*18 (2.3)*	*1.24 (0.66,2.33)*	*0.499*
	Comparison	*1,168*	*22 (1.9)*		
Officer	Ranch Hand	306	10 (3.3)	1.70 (0.68,4.23)	0.256
	Comparison	461	9 (2.0)		
Enlisted Flyer	Ranch Hand	133	5 (3.8)	1.39 (0.39,4.90)	0.608
	Comparison	183	5 (2.7)		
Enlisted Groundcrew	Ranch Hand	333	3 (0.9)	0.59 (0.15,2.23)	0.433
	Comparison	524	8 (1.5)		

Table 11-33. Analysis of Romberg Sign (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,931*	*1.13 (0.59,2.18)*	*0.717*
Officer	767	1.64 (0.64,4.25)	0.304
Enlisted Flyer	313	1.15 (0.31,4.19)	0.837
Enlisted Groundcrew	851	0.56 (0.14,2.18)	0.400

Note: Results were not adjusted for race because of the sparse number of participants with an abnormal Romberg sign.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	4 (2.9)	1.01 (0.64,1.60)	0.961
Medium	143	3 (2.1)		
High	138	4 (2.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	2.11 (1.03,4.34)	0.033*

[a]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with an abnormal Romberg sign.

Table 11-33. Analysis of Romberg Sign (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,168	22 (1.9)		
Background RH	350	7 (2.0)	1.07 (0.45,2.53)	0.886
Low RH	211	6 (2.8)	1.52 (0.61,3.81)	0.367
High RH	210	5 (2.4)	1.27 (0.47,3.40)	0.637
Low plus High RH	421	11 (2.6)	1.39 (0.67,2.90)	0.380

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,163		
Background RH	349	1.00 (0.40,2.48)	0.998
Low RH	210	1.10 (0.42,2.87)	0.841
High RH	208	1.40 (0.48,4.14)	0.538
Low plus High RH	418	1.24 (0.56,2.75)	0.590

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Note: Results were not adjusted for race because of the sparse number of participants with an abnormal Romberg sign.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	5 (1.9)	1.04 (0.78,1.39)	0.799
Medium	257	6 (2.3)		
High	255	7 (2.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 11-33. Analysis of Romberg Sign (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
767	1.44 (0.90,2.32)	0.124

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with an abnormal Romberg sign.

11.2.2.4.4 Gait

Gait was not significantly associated with group or dioxin in the Model 1 through Model 4 unadjusted and adjusted analyses (Table 11-34(a-h): p>0.43 for all analyses).

Table 11-34. Analysis of Gait

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*65 (8.4)*	*1.00 (0.72,1.39)*	*0.984*
	Comparison	*1,169*	*98 (8.4)*		
Officer	Ranch Hand	306	27 (8.8)	1.14 (0.68,1.92)	0.617
	Comparison	461	36 (7.8)		
Enlisted Flyer	Ranch Hand	133	12 (9.0)	0.81 (0.38,1.72)	0.580
	Comparison	183	20 (10.9)		
Enlisted Groundcrew	Ranch Hand	334	26 (7.8)	0.97 (0.58,1.62)	0.909
	Comparison	525	42 (8.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,933*	*0.97 (0.68,1.37)*	*0.861*
Officer	767	1.11 (0.64,1.90)	0.716
Enlisted Flyer	313	0.81 (0.37,1.76)	0.590
Enlisted Groundcrew	853	0.93 (0.54,1.61)	0.788

Table 11-34. Analysis of Gait (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	15 (10.7)	0.92 (0.72,1.17)	0.479
Medium	143	14 (9.8)		
High	138	13 (9.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	0.94 (0.68,1.30)	0.728

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,169	98 (8.4)		
Background RH	351	23 (6.6)	0.85 (0.53,1.36)	0.487
Low RH	211	20 (9.5)	1.11 (0.66,1.84)	0.699
High RH	210	22 (10.5)	1.17 (0.72,1.92)	0.526
Low plus High RH	421	42 (10.0)	1.14 (0.78,1.67)	0.507

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

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Table 11-34. Analysis of Gait (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,164		
Background RH	350	0.83 (0.50,1.36)	0.454
Low RH	210	0.97 (0.57,1.67)	0.919
High RH	208	1.22 (0.70,2.11)	0.481
Low plus High RH	418	1.09 (0.72,1.65)	0.692

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	16 (6.2)	1.06 (0.91,1.25)	0.434
Medium	258	22 (8.5)		
High	255	27 (10.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	0.97 (0.79,1.20)	0.798

[a]Relative risk for a twofold increase in 1987 dioxin.

11.2.2.4.5   CNS Index

A CNS index was constructed and based on a composite variable of tremor, coordination, and gait. This index was coded as "normal" if all three of the components were normal and "abnormal" if otherwise. The Model 1 through Model 4 unadjusted and adjusted analyses showed no significant relation between group or dioxin and the CNS index (Table 11-35(a-h): p>0.18 for all analyses).

Table 11-35. Analysis of CNS Index

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*113 (14.6)*	*0.92 (0.72,1.19)*	*0.533*
	Comparison	*1,169*	*183 (15.7)*		
Officer	Ranch Hand	306	45 (14.7)	1.07 (0.71,1.61)	0.749
	Comparison	461	64 (13.9)		
Enlisted Flyer	Ranch Hand	133	21 (15.8)	0.82 (0.45,1.49)	0.519
	Comparison	183	34 (18.6)		
Enlisted Groundcrew	Ranch Hand	334	47 (14.1)	0.85 (0.58,1.25)	0.402
	Comparison	525	85 (16.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,933*	*0.88 (0.68,1.15)*	*0.359*
Officer	767	1.01 (0.66,1.55)	0.948
Enlisted Flyer	313	0.80 (0.43,1.48)	0.480
Enlisted Groundcrew	853	0.81 (0.54,1.22)	0.315

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	21 (15.0)	1.00 (0.82,1.22)	0.993
Medium	143	24 (16.8)		
High	138	21 (15.2)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	1.09 (0.85,1.41)	0.498

[a]Relative risk for a twofold increase in initial dioxin.

Table 11-35. Analysis of CNS Index (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,169	183 (15.7)		
Background RH	351	47 (13.4)	0.89 (0.63,1.25)	0.495
Low RH	211	29 (13.7)	0.84 (0.55,1.29)	0.424
High RH	210	37 (17.6)	1.09 (0.74,1.61)	0.661
Low plus High RH	421	66 (15.7)	0.96 (0.70,1.31)	0.785

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,164		
Background RH	350	0.88 (0.61,1.27)	0.508
Low RH	210	0.74 (0.47,1.15)	0.183
High RH	208	1.06 (0.69,1.62)	0.796
Low plus High RH	418	0.88 (0.64,1.23)	0.464

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	35 (13.5)	1.05 (0.93,1.19)	0.458
Medium	258	34 (13.2)		
High	255	44 (17.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 11-35. Analysis of CNS Index (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
768	0.98 (0.84,1.15)	0.830

[a]Relative risk for a twofold increase in 1987 dioxin.

11.3 DISCUSSION

The AFHS neurology assessment included the evaluation of cranial nerve function, peripheral nerve status, and CNS coordination processes based on a physical examination. In addition, a cranial nerve index was created by combining responses for the 15 cranial nerve parameters. This index was classified as abnormal if at least one of the determinations was abnormal, and was classified as normal if all of the cranial nerve parameters were normal. The motor and sensory peripheral nerve findings and the cranial nerve examination provide highly specific clues to the anatomic site of possible neurological problems. The various data from the neurology assessment can be relied upon to detect the presence, if not the cause, of neurological disease, particularly disorders of the peripheral nerve system. Pertinent to the current study, the neurological examination was highly sensitive in detecting the presence of peripheral neuropathy, a condition thought to be related to herbicide exposure. The evaluation of CNS coordination processes was based on the presence of tremor, coordination, Romberg sign, and gait, which also are thought to be highly sensitive indicators of herbicide exposure. The neurological evaluations performed in the AFHS were considered sensitive and can be relied upon to detect the presence of peripheral neuropathy.

Dependent variable-covariate analysis confirmed associations with age and diabetes that are well established. Diabetes was by far the strongest covariate and was significantly associated with a history of neurological disease, assessments from the physical examination, and for all the composite indices, particularly those for peripheral neuropathy. Association of neurological endpoints with alcohol use was more sporadic and less prominent.

More Ranch Hand officers than Comparison officers had hereditary and degenerative disease. This result does not appear to be dose-response related, however, as officers had the lowest median value of dioxin and other models did not indicate a dose-response effect.

Based on results from the assessment of the cranial nerves in the neurological examination, more Ranch Hands than Comparisons had abnormal visual fields. The majority of Ranch Hands with abnormal visual fields were in the background dioxin category, and Ranch Hands in the low and high dioxin categories were not significantly different from Comparisons. More Ranch Hands in the low dioxin category had abnormal facial sensation than Comparisons, but the total number of participants with an abnormal facial sensation was small. After adjustment for military occupation, as the initial dioxin level in Ranch Hands increased, the prevalence of abnormal balance increased. More Ranch Hands than Comparisons also had an abnormal cranial nerve index, and this increase was seen in the background and low dioxin categories. There was no dose-response effect, however, within the Ranch Hands. Based on these results, there was no significant clinical evidence of a herbicide or dioxin effect on cranial nerve function.

In assessing the peripheral nerve status of AFHS participants, more Ranch Hands in the high dioxin category had an abnormal pinprick examination. In addition, more Ranch Hands in the high dioxin category and the combined low and high dioxin categories had absent patellar reflexes than Comparisons. As the 1987 dioxin level increased, the prevalence of absent patellar reflex increased as well. More Ranch Hand officers had absent or sluggish Achilles reflexes than Comparison officers, but without evidence of a strong dose-response relation in other occupational cohorts. In addition, no evidence of a strong dose response was found in Models 2 and 4. Although pinprick, balance, and the Achilles reflex are components of the peripheral abnormality index and the peripheral neuropathy indices, these composite indices showed no significant associations.

As in previous studies, there has been some indication for increased risk of peripheral neuropathy in those personnel exposed to the highest level of dioxin. Some indication for an association with probable peripheral neuropathy was found in the 1985, 1992, and 1997 follow-up examinations. Although a dose-response pattern was somewhat inconsistent in those years, the highest risk was observed in the group with the highest dioxin levels, most notably in the 1997 follow-up examination. In the 2002 follow-up examination, Ranch Hands in the high dioxin category had an increased risk for an abnormal pinprick examination and an absent patellar reflex. The risk of an absent patellar reflex increased as the 1987 dioxin level increased.

For the CNS coordination processes, abnormalities in the Romberg sign and the composite index of coordination increased as initial dioxin levels in Ranch Hands increased. Coordination was based on the results of the Romberg sign, finger-nose-finger and heel-knee-shin coordination processes, rapidly alternating movements of pronation and supination of hands, and rapid patting. This result was seen after adjustment for military occupation.

In conclusion, there was no clinical evidence to support a relation between dioxin and cranial nerve function or other CNS processes.

11.4 SUMMARY

The neurology assessment was based on questionnaire data, which was subsequently verified by a review of medical records, and physical examination data. Associations with herbicide exposure (i.e., group – Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable in the neurology assessment. The significant adjusted results are discussed in the sections below.

11.4.1 Model 1: Group Analysis

The results of the group analysis are provided in Table 11-36. Model 1 analyses showed significant differences between all Ranch Hands and Comparisons for visual fields and cranial nerve index. Ranch Hands were more likely to have abnormal visual fields and an abnormal cranial nerve index than Comparisons. When stratified by military occupation, a significant association was seen in officers for hereditary and degenerative diseases and Achilles reflex. More Ranch Hand officers had hereditary or degenerative diseases and sluggish or absent Achilles reflexes than Comparison officers.

Table 11-36. Summary of Group Analysis (Model 1) for Neurology Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Medical Records				
Inflammatory Diseases (D)	NS	NS	NS	NS
Hereditary and Degenerative Diseases (D)	NS	p=0.019 (1.62)	NS	ns
Peripheral Disorders (D)	NS	NS	NS	ns
Other Neurological Disorders (D)	NS	ns	NS	NS
Physical Examination				
Smell (D)	NS	ns	ns	NS
Visual Fields (D)	p=0.040 (2.60)	NS	NS	NS
Light Reaction (D)	ns	ns	--	ns
Ocular Movement (D)	NS	NS	NS	NS
Facial Sensation (D)	NS	NS	ns	NS
Corneal Reflex (D)	ns	ns	ns	ns
Smile (D)	NS	NS	ns	NS
Palpebral Fissure (D)	NS	NS	NS	NS
Balance (D)	NS	NS	NS	ns
Gag Reflex (D)	NS	--	NS	NS
Speech (D)	NS	NS	NS	NS
Tongue Position Relative to Midline (D)	NS	NS	NS	NS
Shoulder Shrug (D)	ns	NS	ns	ns
Cranial Nerve Index (D)	p=0.025 (1.43)	NS	NS	NS
Pinprick (D)	NS	NS	NS	NS
Light Touch (D)	NS	NS	ns	NS
Muscle Status (D)	NS	NS	ns	NS
Patellar Reflex (D)				
Sluggish or Absent vs. Active or Very Active	ns	ns	ns	NS
Absent vs. Sluggish, Active, or Very Active	NS	NS	NS	NS
Achilles Reflex (D)				
Sluggish or Absent vs. Active or Very Active	NS	p=0.013 (1.46)	ns	ns
Absent vs. Sluggish, Active, or Very Active	NS	NS	NS	NS
Biceps Reflex (D)				
Sluggish or Absent vs. Active or Very Active	ns	ns	ns	NS
Absent vs. Sluggish, Active, or Very Active	NS	ns	NS	NS
Babinski Reflex (D)	ns	NS	NS	ns
Any Symmetrical Peripheral Abnormality (D)	NS	NS	NS	NS
Possible Peripheral Neuropathy (D)	NS	NS	NS	NS
Probable Peripheral Neuropathy (D)	NS	NS	NS	ns
Tremor (D)	ns	ns	ns	ns
Coordination (D)	ns	NS	ns	ns
Romberg Sign (D)	NS	NS	NS	ns
Gait (D)	NS	NS	ns	ns
CNS Index (D)	ns	NS	ns	ns

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
      D: Discrete dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

| | ADJUSTED | | | |
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Inflammatory Diseases (D)	NS	NS	NS	NS
Hereditary and Degenerative Diseases (D)	NS	p=0.030 (1.57)	NS	ns
Peripheral Disorders (D)	NS	NS	ns	ns
Other Neurological Disorders (D)	NS	ns	NS	NS
Physical Examination				
Smell (D)	NS	ns	ns	NS
Visual Fields (D)	p=0.022 (3.08)	NS	--	NS
Light Reaction (D)	ns	ns	--	ns
Ocular Movement (D)	NS	NS	--	NS
Facial Sensation (D)	NS	NS	NS	--
Corneal Reflex (D)	ns	ns	--	ns
Smile (D)	NS	ns	NS	NS
Palpebral Fissure (D)	NS	NS	NS	NS
Balance (D)	NS	NS	NS	ns
Gag Reflex (D)	NS	--	NS	--
Speech (D)	NS	NS	--	NS
Tongue Position Relative to Midline (D)	NS	NS	NS	--
Shoulder Shrug (D)	ns	NS	--	ns
Cranial Nerve Index (D)	p=0.020 (1.47)	NS	NS	NS
Pinprick (D)	NS	NS	NS	NS
Light Touch (D)	NS	NS	ns	NS
Muscle Status (D)	NS	NS	ns	NS
Patellar Reflex (D)				
Sluggish or Absent vs. Active or Very Active	ns	ns	ns	NS
Absent vs. Sluggish, Active, or Very Active	NS	NS	NS	NS
Achilles Reflex (D)				
Sluggish or Absent vs. Active or Very Active	NS	p=0.031 (1.42)	ns	ns
Absent vs. Sluggish, Active, or Very Active	NS	NS	NS	NS
Biceps Reflex (D)				
Sluggish or Absent vs. Active or Very Active	NS	ns	ns	NS
Absent vs. Sluggish, Active, or Very Active	NS	ns	NS	NS
Babinski Reflex (D)	ns	NS	NS	ns
Any Symmetrical Peripheral Abnormality (D)	NS	NS	NS	NS
Possible Peripheral Neuropathy (D)	NS	NS	NS	NS
Probable Peripheral Neuropathy (D)	NS	NS	NS	ns

	ADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Tremor (D)	ns	ns	ns	ns
Coordination (D)	ns	ns	ns	ns
Romberg Sign (D)	NS	NS	NS	ns
Gait (D)	ns	NS	ns	ns
CNS Index (D)	ns	NS	ns	ns

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
    D: Discrete dependent variable.

  The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result.

  A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

11.4.2 Model 2: Initial Dioxin Analysis

The results of the initial dioxin analysis are shown in Table 11-37. Model 2 analyses showed a significant inverse association between initial dioxin and smell. Significant positive relations were seen between balance, coordination, and Romberg sign and initial dioxin. Balance and Romberg sign are equivalent, and one of the components of the coordination variable is the Romberg sign.

Table 11-37. Summary of Initial Dioxin Analysis (Model 2) for Neurology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Inflammatory Diseases (D)	NS	NS
Hereditary and Degenerative Diseases (D)	ns	NS
Peripheral Disorders (D)	ns	ns
Other Neurological Disorders (D)	NS	NS
Physical Examination		
Smell (D)	p=0.012 (0.38)	p=0.007 (0.30)
Visual Fields (D)	ns	ns
Light Reaction (D)	p=0.039 (3.98)	NS
Ocular Movement (D)	ns	ns
Facial Sensation (D)	ns	ns
Corneal Reflex (D)	NS	ns
Smile (D)	ns	ns
Palpebral Fissure (D)	NS	NS
Balance (D)	NS	p=0.033 (2.11)
Gag Reflex (D)	ns	ns

Variable	Unadjusted	Adjusted
Speech (D)	ns	ns
Tongue Position Relative to Midline (D)	NS	NS
Shoulder Shrug (D)	ns	ns
Cranial Nerve Index (D)	ns	ns
Pinprick (D)	NS	NS
Light Touch (D)	NS	NS
Muscle Status (D)	NS	NS
Patellar Reflex (D)		
Sluggish or Absent vs. Active or Very Active	ns	NS
Absent vs. Sluggish, Active, or Very Active	NS	NS
Achilles Reflex (D)		
Sluggish or Absent vs. Active or Very Active	ns	NS
Absent vs. Sluggish, Active, or Very Active	ns	NS
Biceps Reflex (D)		
Sluggish or Absent vs. Active or Very Active	ns	ns
Absent vs. Sluggish, Active, or Very Active	NS	NS
Babinski Reflex (D)	ns	NS
Any Symmetrical Peripheral Abnormality (D)	ns	NS
Possible Peripheral Neuropathy (D)	ns	NS
Probable Peripheral Neuropathy (D)	NS	NS
Tremor (D)	NS	NS
Coordination (D)	NS	p=0.002 (2.25)
Romberg Sign (D)	NS	p=0.033 (2.11)
Gait (D)	ns	ns
CNS Index (D)	NS	NS

Note: NS or ns: Not significant (p>0.05).

      D: Discrete dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

11.4.3 Model 3: Categorized Dioxin Analysis

The results of the categorized dioxin analysis are presented in Table 11-38. More Ranch Hands in the background dioxin category than Comparisons showed abnormal visual fields and an abnormal cranial nerve index. More Ranch Hands in the low dioxin category than Comparisons showed an abnormal facial sensation and an abnormal cranial nerve index. More Ranch Hands in the high dioxin category had an abnormal reaction to pinprick and absent patellar reflexes than Comparisons. This difference in patellar reflexes was also seen in the low and high dioxin categories combined.

Table 11-38. Summary of Categorized Dioxin Analysis (Model 3) for Neurology Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Inflammatory Diseases (D)	NS	NS	NS	NS
Hereditary and Degenerative Diseases (D)	NS	NS	NS	NS
Peripheral Disorders (D)	NS	NS	NS	NS
Other Neurological Disorders (D)	ns	NS	p=0.005 (1.65)	p=0.002 (1.53)
Physical Examination				
Smell (D)	NS	NS	ns	ns
Visual Fields (D)	p=0.005 (4.37)	NS	NS	NS
Light Reaction (D)	NS	ns	ns	ns
Ocular Movement (D)	NS	NS	NS	NS
Facial Sensation (D)	ns	p=0.033 (5.74)	ns	NS
Corneal Reflex (D)	ns	ns	NS	ns
Smile (D)	ns	NS	ns	NS
Palpebral Fissure (D)	NS	NS	NS	NS
Balance (D)	NS	NS	NS	NS
Gag Reflex (D)	ns	NS	NS	NS
Speech (D)	NS	ns	NS	NS
Tongue Position Relative to Midline (D)	ns	NS	NS	NS
Shoulder Shrug (D)	ns	NS	ns	NS
Cranial Nerve Index (D)	p=0.019 (1.61)	p=0.027 (1.69)	ns	NS
Pinprick (D)	NS	ns	p=0.020 (1.76)	NS
Light Touch (D)	ns	ns	NS	NS
Muscle Status (D)	NS	NS	NS	NS
Patellar Reflex (D)				
Sluggish or Absent vs. Active or Very Active	ns	NS	ns	NS
Absent vs. Sluggish, Active, or Very Active	ns	NS	NS	p=0.025 (1.84)
Achilles Reflex (D)				
Sluggish or Absent vs. Active or Very Active	NS	NS	ns	NS
Absent vs. Sluggish, Active, or Very Active	NS	p=0.029 (1.45)	NS	NS
Biceps Reflex (D)				
Sluggish or Absent vs. Active or Very Active	ns	NS	ns	NS
Absent vs. Sluggish, Active, or Very Active	ns	NS	NS	NS
Babinski Reflex (D)	NS	ns	ns	ns
Any Symmetrical Peripheral Abnormality (D)	NS	p=0.027 (1.46)	NS	NS
Possible Peripheral Neuropathy (D)	NS	p=0.034 (1.45)	NS	NS
Probable Peripheral Neuropathy (D)	NS	NS	NS	NS

	UNADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Tremor (D)	ns	ns	NS	ns
Coordination (D)	ns	ns	ns	ns
Romberg Sign (D)	NS	NS	NS	NS
Gait (D)	ns	NS	NS	NS
CNS Index (D)	ns	ns	NS	ns

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
     D: Discrete dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

	ADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Medical Records				
Inflammatory Diseases (D)	NS	NS	NS	NS
Hereditary and Degenerative Diseases (D)	NS	NS	NS	NS
Peripheral Disorders (D)	NS	NS	ns	NS
Other Neurological Disorders (D)	NS	NS	NS	NS
Physical Examination				
Smell (D)	NS	NS	--	--
Visual Fields (D)	p=0.004 (5.25)	NS	NS	NS
Light Reaction (D)	NS	--	ns	--
Ocular Movement (D)	NS	NS	NS	NS
Facial Sensation (D)	NS	p=0.033 (7.94)	--	--
Corneal Reflex (D)	ns	--	NS	--
Smile (D)	ns	NS	NS	NS
Palpebral Fissure (D)	NS	NS	NS	NS
Balance (D)	NS	NS	NS	NS
Gag Reflex (D)	--	NS	NS	NS
Speech (D)	NS	NS	NS	NS
Tongue Position Relative to Midline (D)	--	NS	NS	NS
Shoulder Shrug (D)	ns	NS	--	--
Cranial Nerve Index (D)	p=0.018 (1.65)	p=0.049 (1.62)	NS	NS
Pinprick (D)	NS	ns	p=0.050 (1.71)	NS
Light Touch (D)	ns	ns	NS	NS
Muscle Status (D)	NS	NS	NS	NS

	ADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Patellar Reflex (D)				
Sluggish or Absent vs. Active or Very Active	ns	NS	NS	NS
Absent vs. Sluggish, Active, or Very Active	ns	NS	p=0.048 (2.11)	p=0.027 (1.89)
Achilles Reflex (D)				
Sluggish or Absent vs. Active or Very Active	NS	NS	NS	NS
Absent vs. Sluggish, Active, or Very Active	NS	NS	NS	NS
Biceps Reflex (D)				
Sluggish or Absent vs. Active or Very Active	ns	NS	ns	NS
Absent vs. Sluggish, Active, or Very Active	ns	ns	NS	NS
Babinski Reflex (D)	NS	ns	ns	ns
Any Symmetrical Peripheral Abnormality (D)	NS	NS	NS	NS
Possible Peripheral Neuropathy (D)	NS	NS	NS	NS
Probable Peripheral Neuropathy (D)	NS	ns	NS	NS
Tremor (D)	ns	ns	NS	ns
Coordination (D)	ns	ns	ns	ns
Romberg Sign (D)	NS	NS	NS	NS
Gait (D)	ns	ns	NS	NS
CNS Index (D)	ns	ns	NS	ns

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant ($p>0.05$).
       D: Discrete dependent variable.

       The p-value was given if $p \leq 0.05$. The relative risk was given in parentheses for a significant result.

       A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

11.4.4 Model 4: 1987 Dioxin Level Analysis

The results of the 1987 dioxin analysis are displayed in Table 11-39. Model 4 analyses showed a significant inverse association between 1987 dioxin level and smell, and showed a significant positive association with the absence of the patellar reflex.

Table 11-39. Summary of 1987 Dioxin Analysis (Model 4) for Neurology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Inflammatory Diseases (D)	ns	ns
Hereditary and Degenerative Diseases (D)	ns	NS
Peripheral Disorders (D)	NS	NS
Other Neurological Disorders (D)	p=0.007 (1.16)	NS
Physical Examination		
Smell (D)	p=0.018 (0.71)	p=0.010 (0.64)
Visual Fields (D)	ns	ns
Light Reaction (D)	NS	NS
Ocular Movement (D)	ns	ns
Facial Sensation (D)	ns	NS
Corneal Reflex (D)	NS	NS
Smile (D)	NS	NS
Palpebral Fissure (D)	NS	NS
Balance (D)	NS	NS
Gag Reflex (D)	NS	NS
Speech (D)	ns	ns
Tongue Position Relative to Midline (D)	NS	NS
Shoulder Shrug (D)	ns	ns
Cranial Nerve Index (D)	ns	ns
Pinprick (D)	NS	NS
Light Touch (D)	NS	NS
Muscle Status (D)	ns	ns
Patellar Reflex (D)		
Sluggish or Absent vs. Active or Very Active	NS	NS
Absent vs. Sluggish, Active, or Very Active	p=0.017 (1.29)	p=0.013 (1.44)
Achilles Reflex (D)		
Sluggish or Absent vs. Active or Very Active	ns	ns
Absent vs. Sluggish, Active, or Very Active	NS	NS
Biceps Reflex (D)		
Sluggish or Absent vs. Active or Very Active	NS	NS
Absent vs. Sluggish, Active, or Very Active	NS	NS
Babinski Reflex (D)	ns	ns
Any Symmetrical Peripheral Abnormality (D)	NS	NS
Possible Peripheral Neuropathy (D)	NS	NS
Probable Peripheral Neuropathy (D)	NS	ns
Tremor (D)	NS	NS
Coordination (D)	NS	NS
Romberg Sign (D)	NS	NS
Gait (D)	NS	ns
CNS Index (D)	NS	ns

Note: NS or ns: Not significant (p>0.05).
        D: Discrete dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

11.4.5 Summary of Significant Results

Table 11-40 summarizes the significant results (p≤0.05) for the adjusted analyses that were performed for the neurology assessment. The dependent variable and its table reference are listed, along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and explained in footnotes.

Table 11-40. Summary of Results from Significant Adjusted Analyses in the Neurology Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Percent Abnormal	Note
Hereditary and Degenerative Diseases (11-4)	1	RH vs. C, Officer	0.030	1.57 (1.04,2.36)	RH: 18.6% C: 12.4%	(a)
Smell (11-7)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.007	0.30 (0.10,0.89)	Low: 3.6% Medium: 2.1% High: 0.0%	(b)
	4	All RH: 1987 Dioxin	0.010	0.64 (0.45,0.90)	Low: 4.6% Medium: 2.7% High: 0.8%	(c)
Visual Fields (11-8)	1	RH vs. C, All	0.022	3.08 (1.13,8.41)	RH: 1.6% C: 0.6%	(a)
	3	Background RH vs. C	0.004	5.25 (1.71,16.13)	RH: 2.3% C: 0.6%	(d)
Facial Sensation (11-11)	3	Low RH vs. C	0.033	7.94 (1.19,53.10)	RH: 1.4% C: 0.3%	(d)
Balance (11-15)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.033	2.11 (1.03,4.34)	Low: 2.9% Medium: 2.1% High: 2.9%	(b)
Cranial Nerve Index (11-20)	1	RH vs. C, All	0.020	1.47 (1.06,2.04)	RH: 10.7% C: 7.7%	(a)
	3	Background RH vs. C	0.018	1.65 (1.09,2.50)	RH: 11.5% C: 7.7%	(d)
	3	Low RH vs. C	0.049	1.62 (1.00,2.61)	RH: 12.4% C: 7.7%	(d)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Percent Abnormal	Note
Pinprick (11-21)	3	High RH vs. C	0.050	1.71 (1.00,2.93)	RH: 15.3% C: 8.9%	(d)
Patellar Reflex (11-24)	3	High RH vs. C – Absent vs. Very Active, Active, or Sluggish	0.048	2.11 (1.01,4.43)	RH: 5.7% C: 3.0%	(d)
	3	Low and High RH vs. C – Absent vs. Very Active, Active, or Sluggish	0.027	1.89 (1.07,3.33)	RH: 5.7% C: 3.0%	(d)
	4	All RH: 1987 Dioxin – Absent vs. Very Active, Active, or Sluggish	0.013	1.44 (1.07,1.95)	Low: 2.3% Medium: 5.5% High: 5.1%	(c)
Achilles Reflex (11-25)	1	RH vs. C, Officer – Sluggish or Absent vs. Very Active or Active	0.031	1.42 (1.03,1.95)	RH: 66.0% C: 57.1%	(a)
Coordination (11-32)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.002	2.25 (1.30,3.90)	Low: 2.9% Medium: 2.1% High: 5.8%	(b)
Romberg Sign (11-33)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.033	2.11 (1.03,4.34)	Low: 2.9% Medium: 2.1% High: 2.9%	(b)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal was presented for each of three initial dioxin categories.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

Note: RH = Ranch Hand.
          C = Comparison.

   Model 2:   Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt).

   Model 3:   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
              Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
              High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

   Model 4:   Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

11.5   CONCLUSION

The AFHS neurology assessment included the evaluation of cranial nerve function, peripheral nerve status, and CNS coordination processes based on a physical examination. The motor and sensory peripheral nerve findings and the cranial nerve examination provided specific clues to the anatomic site of possible neurological problems. The neurological evaluations performed in the AFHS were sensitive, and can be relied upon to detect the presence of peripheral neuropathy. These results are summarized below by statistical model.

With regard to group contrasts, Ranch Hands were more likely to have abnormal visual fields and an abnormal cranial nerve index than Comparisons. More Ranch Hand officers had hereditary or degenerative diseases and sluggish or absent Achilles reflexes than Comparison officers.

Significant positive relations were seen between balance and coordination and extrapolated initial dioxin levels.

Analyses based on dioxin category showed an increased risk of abnormal visual fields in the background dioxin category and an increased risk of abnormal facial sensation for Ranch Hands in the low dioxin category. Ranch Hands in both the background and low dioxin categories showed an increased risk of abnormalities for the cranial nerve index, a composite index of the individual 15 cranial nerve endpoints studied in this assessment. More Ranch Hands in the high dioxin category had an abnormal reaction to pinprick and absent patellar reflexes than Comparisons.

Analyses of 1987 dioxin levels showed a significant positive association with the absence of the patellar reflex.

Based on the results of the analysis of pinprick, balance, and the patellar reflex in this follow-up examination, there was some limited support of an association between dioxin levels and neurological disease related to the peripheral nerves. In conclusion, there was no clinical evidence to support a relation between dioxin and cranial nerve function or other CNS processes.

REFERENCES

1. Institute of Medicine. 2003. Veterans and Agent Orange: Update 2002. National Academy Press: Washington, DC.

2. Kakeyama, M. and C. Tohyama. 2003. Developmental neurotoxicity of dioxin and its related compounds. *Industrial Health* 41:215-30.

3. Sirkka, U., R. Pohjanvirta, S.A. Nieminen, J. Tuomisto, and P. Ylitalo. 1992. Acute neurobehavioral effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in Han/Wistar rats. *Pharmacology and Toxicology* 71:284-8.

4. Pohjanvirta, R., L. Tuomisto, and J. Tuomisto. 1989. The central nervous system may be involved in TCDD toxicity. *Toxicology* 58:167-74.

5. Silbergeld, E.K., and S.R. Max. 1986. Neuromuscular targets for the action of 2,3,7,8-TCDD. Abstract of a paper presented at the 6th International Symposium on Chlorinated Dioxins and Related Compounds, September 16-19, Fukuoka, Japan.

6. Grahmann, F., D. Claus, H. Grehl, and B. Neundorfer. 1993. Electrophysiologic evidence for a toxic polyneuropathy in rats after exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Journal of the Neurological Sciences* 115(1):71-5.

7. Grehl, H., F. Grahmann, D. Claus, and B. Neundorfer. 1993. Histologic evidence for a toxic polyneuropathy due to exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in rats. *Acta Neurologica Scandinavica* 88:354-7.`

8. Mattsson, J.L., and D.L. Eisenbrandt. 1990. The improbable association between the herbicide 2,4-D and polyneuropathy. *Biomedical and Environmental Sciences* 3:43-51.

9. Klawans, H.L. 1987. Dystonia and tremor following exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Movement Disorders* 2:255-61.

10. Oliver, R.M. 1975. Toxic effects of 2,3,7,8-tetrachlorodibenzo-1,4-dioxin in laboratory workers. *British Journal of Industrial Medicine* 32:49-53.

11. Singer, R., M. Moses, J. Valciukas, R. Lilis, and I.J. Selikoff. 1982. Nerve conduction velocity studies of workers employed in the manufacture of phenoxy herbicides. *Environmental Research* 29:297-311.

12. Moses, M., R. Lilis, K.D. Crow, J. Thornton, A. Fischbein, H.A. Anderson, and I.J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *American Journal of Industrial Medicine* 5:161-82.

13. Suskind, R.R., and V.S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *The Journal of the American Medical Association* 251:2372-80.

14. Pazderova-Vejlupkova, J., M. Nemcova, J. Pickova, L. Jirasek, and E. Lukas. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Archives of Environmental Health* 36:5-11.

15. Sweeney, M.H., M.A. Fingerhut, J.C. Arezzo, R.W. Hornung, and L.B. Connally. 1993. Peripheral neuropathy after occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *American Journal of Industrial Medicine* 23:845-58.

16. Cheng, W.N., P.J. Coenraads, Z.H. Hao, and G.F. Liu. 1993. A health survey of workers in the pentachlorophenol section of a chemical manufacturing plant. *American Journal of Industrial Medicine* 24:81-92.

17. Webb, K.B., R.G. Evans, P.A. Stehr, and S.M. Ayres. 1987. Pilot study on health effects of environmental 2,3,7,8-TCDD in Missouri. *American Journal of Industrial Medicine* 11:685-91.

18. Webb, K.B., R.G. Evans, A.P. Knutsen, S.T. Roodman, D.W. Roberts, W.F. Schramm, B.B. Gibson, J.S. Andrews, Jr., L.L. Needham, and D.G. Patterson. 1989. Medical evaluation of subjects with known body levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 28:183-93.

19. Hoffman, R.E., P.A. Stehr-Green, K.B. Webb, R.G. Evans, A.P. Knutsen, W.F. Schramm, B.B. Gibson, and K.K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *The Journal of the American Medical Association* 225:2031-8.

20. Stehr, P.A., G. Stein, H. Falk, E. Sampson, S.J. Smith, K. Steinberg, K. Webb, S. Ayres, W.F. Schramm, H.D. Donnell, and W.B. Gedney. 1986. A pilot epidemiologic study of possible health effects associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin contaminations in Missouri. *Archives of Environmental Health* 41:16-22.

21. Stehr-Green, P.A., J.S. Andrews, Jr., R.E. Hoffman, K.B. Webb, and W.F. Schramm. 1988. An overview of the Missouri dioxin studies. *Archives of Environmental Health* 43:174-7.

22. Filippini, G., B. Bordo, P. Crenna, N. Massetto, M. Musicco, and R. Boeri. 1981. Relationship between clinical and electrophysiological findings and indicators of heavy exposure to 2,3,7,8-tetrachlorodibenzo-dioxin. *Scandinavian Journal of Work, Environment and Health* 7:257-62.

23. Bertazzi, P.A. 1991. Long-term effects of chemical disasters. Lessons and results from Seveso. *Science of the Total Environment* 106:5-20.

24. Boeri, R., B. Bordo, P. Crenna, G. Filippini, M. Massetto, and A. Zecchini. 1978. Preliminary results of a neurological investigation of the population exposed to TCDD in the Seveso region. *Rivista di Patologia Nervosa e Mentale* 99:111-28.

25. Barbieri, S., C. Pirovano, G. Scarlato, P. Tarchini, A. Zappa, and M. Maranzana. 1988. Long-term effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on the peripheral nervous system. Clinical and neurophysiological controlled study on subjects with chloracne from the Seveso area. *Neuroepidemiology* 7:29-37.

26. Zober, A., M. G. Ott, and P. Messerer. 1994. Morbidity followup study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

27. Assennato, G., D. Cervino, E.A. Emmett, G. Longo, and F. Merlo. 1989. Followup of subjects who developed chloracne following TCDD exposure at Seveso. *American Journal of Industrial Medicine* 16:119-25.

28. Morcarelli, P., A. Marocchi, P. Brambilla, P. Gerthoux, C. Beretta, L. Colombo, M. Bertona, C. Sarto, P. Tramacere, A. Mondonico, C. Crespi, S. Signorini, and R. Brivio. 1992. Human data derived from the Seveso accident, relevance for human risk assessment. *Toxic Substances Journal* 12:151-73.

29. Stellman, S.D., J.M. Stellman, and J.F. Sommer, Jr. 1988. Health and reproductive outcomes among American Legionnaires in relation to combat and herbicide exposure in Vietnam. *Environmental Research* 47:150-74.

30. Centers for Disease Control. 1988. Health status of Vietnam veterans. II. Physical health. *The Journal of the American Medical Association* 259:2708-14.

31. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline Morbidity Study Results. NTIS: AD A 138-340. USAF School of Medicine, Brooks Air Force Base, TX.

32. Lathrop, G.D., S.G. Machado, T.G. Karrison, W.D. Grubbs, W.F. Thomas, W.H. Wolfe, J.E. Michalek, J.C. Miner, and M.R. Peterson. 1987. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188 262. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

33. Thomas, W.F., W.D. Grubbs, T.G. Karrison, M.B. Lustik, R.H. Roegner, D.E. Williams, W.H. Wolfe, J.E. Michalek, J.C. Miner, and R.W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

34. Grubbs, W.D., W.H. Wolfe, J.E. Michalek, D.E. Williams, M.B. Lustik, A.S. Brockman, S.C. Henderson, F.R. Burnett, R.G. Land, D.J. Osborne, V.K. Rocconi, M.E. Schreiber, J.C. Miner, G.L. Henriksen, and J.A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1992 followup examination results. NTIS: AD A 304 306, 304 308-316. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

35. Roegner, R.H., W.D. Grubbs, M.B. Lustik, A.S. Brockman, S.C. Henderson, D.E. Williams, W.H. Wolfe, J.E. Michalek, and J.C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides. Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

36. Kim, J.S., H.S. Lim, S.I. Cho, H.K. Cheong, and M.K. Lim. 2003. Impact of Agent Orange exposure among Korean Vietnam veterans. *Industrial Health* 41:149-57.

37. Sweeney, M.H., and P. Mocarelli. 2000. Human health effects after exposure to 2,3,7,8-TCDD. *Food Additives and Contaminants* 17:303-16.

38. Neuberger, M., C. Rappe, S. Bergek, H. Cai, M. Hansson, R. Jager, M. Kundi, C.K. Lim, H. Wingfors, and A.G. Smith. 1999. Persistent health effects of dioxin contamination in herbicide production. *Environmental Research* 81(3): 206-14.

39. Pelclová, D., Z. Fenclová, Z. Dlaskova, P. Urban, E. Lukás, B. Procházka, C. Rappe, J. Preiss, A. Kocan, J. Vejlupkova. 2001. Biochemical, neuropsychological, and neurological abnormalities following 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure. *Archives of Environmental Health* 56:493-500.

40. Institute of Medicine. 2001. Veterans and Agent Orange: Update 2000. National Academy Press: Washington, DC.

41. Institute of Medicine. 1999. Veterans and Agent Orange: Update 1998. National Academy Press: Washington, DC.

42. Institute of Medicine. 1997. Veterans and Agent Orange: Update 1996. National Academy Press: Washington, DC.

43. Michalek, J.E, F.Z. Akhtar, J.C. Arezzo, D.H. Garabrant, and J.W. Albers. 2001. Serum dioxin and peripheral neuropathy in veterans of Operation Ranch Hand. *Neurotoxicology* 22:479-90.

44. Garrow, J.S., and J. Webster. 1985. Quetelet's index (W/H^2) as a measure of fatness. *International Journal of Obesity* 9:147-53.

45. Patterson, D.G., Jr., L. Hampton, C R. Lapeza, Jr., W.T. Belser, V. Green, L.R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

46. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57:369-78.

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12.1 INTRODUCTION

12.1.1 Background

12.1.1.1 Organs/Diseases

The Symptom Checklist-90-Revised (SCL-90-R) (1) and the Wechsler Memory Scale-Revised (WMS-R) (2) were used in the psychology assessment of participants in the Air Force Health Study (AFHS). The SCL-90-R was used to measure symptomatic psychological distress in terms of anxiety, depression, hostility, interpersonal sensitivity, obsessive-compulsive behavior, paranoid ideation, phobic anxiety, psychoticism, and somatization. The SCL-90-R was also used to measure three global distress indices: global severity index (GSI), positive symptom total (PST), and positive symptom distress index (PSDI). The WMS-R is an instrument used for appraising major dimensions of memory functions in adolescents and adults, including memory for verbal and figural stimuli, meaningful and abstract material, and delayed as well as immediate recall. Psychological disorders as verified through medical records review, such as psychoses, alcohol and drug dependence, anxiety, and other neuroses, were studied to supplement the psychological evaluation.

12.1.1.2 Toxicology

Signs of dioxin neurotoxicity in animals (e.g., lethargy, stupor, poor coordination, lack of feeding, and agitation) were observed in multiple studies in many species and have been attributed to the "wasting syndrome" of multi-organ toxicity rather than to primary central nervous system (CNS) involvement (3). Pharmacokinetic studies in rats (4), mice (5), and monkeys (6) demonstrated that the blood-brain barrier is relatively impermeable to dioxin; therefore, experimental animal studies provide little insight into the potential neuropsychological consequences of dioxin in humans.

In rats exposed to high doses of dioxin (1,000 micrograms intraperitoneally), only slight differences were noted in spontaneous motor activity and maze performance relative to controls (7). A study from the same laboratory found no neurobehavioral impairment in rats given a sublethal dose of dioxin sufficient to cause the wasting syndrome (8). These findings were supported in recent studies showing that alterations in cognitive function in rats, if any, after dioxin exposure early in life were very subtle (9, 10). In a recent report, rats exposed to dioxin during gestation and lactation also showed very subtle effects on cognitive function (11). In contrast, experiments in monkeys documented "subtle" behavioral dysfunction and cognitive impairment consequent to dioxin exposure in utero (12-15).

12.1.1.3 Epidemiology

Numerous studies were published describing psychological sequelae in populations exposed to dioxin through environmental contamination, industrial accidents, occupation, and in association with service in Southeast Asia (SEA) during the Vietnam War.

A limited number of epidemiologic studies (16-18) examined neurobehavioral health effects of environmental exposure to dioxin. Neuropsychiatric testing was included in the medical evaluations reported in two studies of 154 mobile home park residents exposed to dioxin by contaminated soil in Quail Run, Missouri (16, 17). Relative to 155 unexposed controls residing at similar mobile home parks

without dioxin contamination, exposed subjects had poorer scores on the tension or anxiety and anger or hostility scales of the Profile of Mood States Inventory, as well as in the vocabulary subtest of the Wechsler Adult Intelligence Scale (WAIS) (19). Furthermore, the exposed group performed worse on the depression/dejection and fatigue/inertia scales relative to unexposed controls (17).

A small study in Germany evaluated the neuropsychological effects of chronic exposure to dioxins among 19 persons exposed to environmental contamination from a metal reclamation plant (18). Subjects were compared according to blood levels of dioxins and furans below and above the median exposure level in the study population. A substantial proportion of subjects reported irritability (42%), depressed feelings (37%), and fatigue (44%). Irritability and depressed feelings were more frequently reported by those with exposure levels above the median relative to those with lower exposures.

Some occupational studies investigated the potential neuropsychological effects of dioxin exposure, but few studies related serum dioxin levels to neuropsychological indices. Early studies of industrial chemical workers provided the first suggestion of associated psychological effects using chloracne as a marker for high-level dioxin exposure. Studies conducted shortly after the Nitro, West Virginia, accident in 1949 documented nervousness, fatigue, irritability, cold intolerance, and decreased libido in many of the workers with chloracne. Most of these symptoms resolved over a 4-year period (20, 21). In addition, two follow-up studies were conducted of expanded Nitro plant cohorts in 1979 (22, 23). Moses and colleagues, in a cross-sectional health survey, found chloracne in 52 percent of 226 workers. Differences in the prevalence of insomnia and decreased libido were observed between the groups with and without chloracne (22). Similar findings were reported in another investigation of 204 exposed and 163 unexposed workers, with a higher prevalence of nervousness and decreased libido in the exposed group (23).

Other industrial-based studies reported a wide range of acute and subacute symptoms associated with exposure to chlorophenols. In addition to those cited above, impotence, reduced emotional responses, sensory deficits, reading difficulties, memory loss, and emotional instability were described (24-29). Employing the Minnesota Multiphasic Personality Inventory (MMPI) (30), an early study of 73 male chemical production workers found an exposure-response association between the development of chloracne and hypomania, and a significantly increased incidence of personality disorders in those employees most heavily exposed (28). Furthermore, a case report described marked personality changes in two of three chemists involved in the synthesis of dioxin (29). Yet another study of 55 Czechoslovakian workers with dioxin intoxication initially found a significant prevalence of encephalopathy (7%) and neurasthenia (75%) among the workers. Over time, the prevalence of psychic disturbances decreased substantially (27). In a recent follow-up study of 13 workers in this cohort, plasma dioxin levels were negatively correlated with the memory quotient from the WMS, the verbal intelligence quotient (IQ) from the WAIS-Revised (31), and the Benton Revised Visual Retention Test (32-34).

The National Institute for Occupational Safety and Health's (NIOSH's) study of chemical plant workers is one of a few epidemiologic studies in humans that incorporates serum dioxin data into psychometric analyses (35). This cross-sectional study of 281 exposed workers in two industrial plants and 260 unexposed community controls investigated the association between exposure to chemicals (including dioxin) and symptoms of depression based on a battery of psychological screening tests (the Beck Depression Inventory and the depression subscale of the SCL-90-R). The mean serum dioxin level in the exposed cohort was 220 parts per trillion (ppt) versus 6 ppt in referents. By both scales, the prevalence of depression was comparable in each group. No association between dioxin exposure and scores in the two psychological tests was found based on either group membership or serum exposure levels.

In a morbidity follow-up study of 158 men exposed to dioxin after a chemical accident at the trichlorophenol unit of a BASF chemical facility, the rate of episodes of illness among exposed workers was compared to the rate in an unexposed population employed at the same facility (36). Exposure to dioxin was determined based on chloracne status and extrapolated blood lipid concentrations. An increase was found in episodes of mental disorders (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] 290-317) among those with severe chloracne; however, no association with dioxin levels in the blood was observed.

The association between psychological symptoms and reported herbicide exposure during military service in Vietnam has been the subject of several studies (37-39). Some studies have focused on dioxin exposure specifically (40-45). In one study of 153 veterans who reported at least a 5-year history of continuous daily drug abuse, a subgroup of 58 subjects reporting moderate to high herbicide exposure had MMPI scores that indicated depression, poor morale, organic symptoms, family problems, and hypomania compared to the remaining 95 veterans (37). In another study of 7,924 U.S. Army veterans, those with Vietnam experience were at increased risk of psychological problems and illicit drug use as compared to non-Vietnam veterans (38). Among Vietnam veterans, the level of reported herbicide exposure was related to unfavorable mental health outcomes in an exposure-response fashion (38). Some evidence from the Vietnam Experience Study, conducted by the Centers for Disease Control and Prevention (CDC), indicates that service in Vietnam may be associated with psychological morbidity independent of exposure to herbicides (39). A recent study of 1,224 Korean Vietnam veterans found insufficient evidence for an increased prevalence of psychiatric disorders (46).

The evidence for an association between serum dioxin levels and cognitive functioning among Ranch Hand personnel in the AFHS was recently evaluated (40, 45). Cognitive functioning was assessed in 1982 using the WAIS-Revised, the WMS, the Halstead-Reitan Neuropsychological Test Battery (HRB) (47), and the Wide Range Achievement Test (48). In addition, information was collected on psychiatric diagnoses and psychotropic medication use during the 1982 physical examination. Each veteran was assigned to a background, low, or high dioxin exposure category based on serum dioxin levels determined in 1987 and 1992. There was no consistent effect of dioxin exposure on cognitive functioning, and dose-response gradients were generally absent. Although several measures of memory functioning were decreased among those with the highest dioxin levels, the differences were considered relatively small and of unknown clinical relevance (40).

Other reports of the AFHS also found inconclusive evidence for an association between psychological indices and dioxin exposure among Ranch Hands (41-44). The 1987 examinations suggested an association between serum dioxin levels and some scales on the Millon Clinical Multiaxial Inventory (MCMI) (49), but there was no evidence for a relation with indices on the SCL-90-R (44). In the analysis of the 1997 follow-up examination results, a dose-response pattern between 1987 dioxin concentrations and the prevalence of other neuroses among Ranch Hands was limited to the enlisted groundcrew, the subgroup with the highest dioxin levels (41). Otherwise, few significant associations were found (50). Similarly, Michalek and colleagues found little evidence for an association between serum dioxin levels and psychological functioning determined by the MMPI and the MCMI among Ranch Hand veterans (45).

In the 2002 report published by the Institute of Medicine (50), the committee concluded that there is "inadequate or insufficient" evidence of an association between exposure to certain herbicides used in Vietnam and cognitive or neuropsychiatric disorders.

12.1.2 Summary of Previous Analyses of the Air Force Health Study

12.1.2.1 1982 Baseline Examination Summary Results

An extensive battery of psychological parameters was assessed on all participants during the 1982 baseline questionnaire and as part of the physical examination process. There were no questionnaire differences for past history of emotional or psychological illnesses between the Ranch Hand and Comparison groups. For the psychological indices of fatigue, anger, erosion of skills, anxiety, and severity of depression, no group differences were detected among the college-educated Ranch Hands. For the high school-educated stratum, Ranch Hands demonstrated significantly more fatigue, anger, erosion of skills, and anxiety. An analysis of the isolation index adjusted for education level showed significantly higher (adverse) scores in the Ranch Hand group. The isolation index was based on the answers to three questions that are related to the amount of activity that the participant has with friends, relatives, and community.

At the time of the physical examination, additional data were collected with the Cornell Index (CI) (51) and the MMPI. The CNS functional testing was conducted by a modified HRB and intelligence was measured by the WAIS.

The CI showed a significant increase in psychophysiological symptoms in the high school-educated Ranch Hands. MMPI results in the high school-educated participants showed Ranch Hand mean values significantly increased in the scales of denial, hypochondria, masculinity-femininity, and mania-hypomania. The social introversion scale was significantly decreased in the college-educated Ranch Hands. None of the self-reported data, including those from the in-home questionnaire, was adjusted for possible group differences in post-traumatic stress disorder (PTSD) or combat experience and intensity.

Performance testing by the HRB showed no neuropsychiatric impairment in the Ranch Hands in contrast to the results of the self-administered MMPI and the CI. WAIS intelligence scores revealed group similarities in the full-scale and verbal and performance scales. The IQ of the college-educated participants was significantly higher than the IQ of the high school-educated participants.

12.1.2.2 1985 Follow-up Examination Summary Results

Two of the psychological tests (MMPI, HRB) conducted at the 1982 baseline examination were repeated at the first follow-up examination in 1985. An updated history of mental and emotional disorders and combat experience in Vietnam also was obtained on all participants. An indicator of PTSD was derived from a new MMPI subscale and was used for covariate adjustments of non-MMPI psychological data. The Cornell Medical Index (CMI) (52) was substituted for the CI in the 1985 psychology assessment. Higher scores on these instruments may reflect an adverse condition in the psychological health of the participant. Questionnaire data (verified by a medical records review) for the lifetime events of psychotic illness, alcohol dependence, anxiety, or other neuroses disclosed no significant differences between groups for these conditions.

The group distributions for the 14 MMPI variables, each stratified by the three occupational categories, were examined. Ranch Hand enlisted flyers had a lower psychopathic deviate mean than Comparison enlisted flyers, and Ranch Hand officers had a higher mania/hypomania mean than Comparison officers. The group distributions of the total CMI score were similarly contrasted, with separate analyses performed with stratification by the five covariates of age, race, occupation, education, and current alcohol drinking status. For one stratum of each of these covariates (born in or after 1942, non-Black, enlisted groundcrew, high school education, and current alcohol drinker), a significant difference in the distribution of the Ranch Hand and Comparison scores was found. In all cases for the CMI, the Ranch

Hand mean was greater than the Comparison mean, suggesting more illness for Ranch Hands relative to Comparisons.

The adjusted analyses of the MMPI scales of denial and masculinity-femininity were statistically significant, where Comparisons showed an adverse effect over Ranch Hands. Ranch Hands had significantly higher mean scores than Comparisons on the A-H area subscore of the CMI, suggesting that Ranch Hands had more diffuse medical problems. The M-R subscore of the CMI, a broad indicator of emotional health, was not statistically different between the two groups.

The HRB impairment index, a measure of CNS functional integrity, did not differ significantly between the Ranch Hand and Comparison groups.

Because of interactions in models and slightly different psychological testing parameters, a direct contrast between the psychological results of the baseline and 1985 follow-up examinations was not always possible. Several broad patterns, however, were observed: (1) the discordance between distributional tests and results from traditional statistical models of the MMPI variables was noted with data from both examinations; (2) there was a narrowing of group differences at the 1985 follow-up examination for most variables, either by a decrease in Ranch Hand reporting or by an increase in Comparison reporting; and (3) as at the baseline examination, functional CNS testing, as measured by the HRB impairment index, showed no group differences and did not support an organic basis for differences in self-reported symptomatology. The longitudinal analysis of two MMPI scales—depression and denial—showed a significant reversal of depression seen at the baseline examination in the high school-educated Ranch Hands. The number of depression abnormalities decreased in Ranch Hands and increased in Comparisons.

The determination of PTSD in both Air Force cohorts by a relatively new MMPI scale showed a prevalence rate of less than 1 percent. This low rate was strongly influenced by characteristics of the study population (e.g., age, education, and military occupation).

In conclusion, significant test results were present in both groups or were noted in specific subgroups of a covariate. Tests of the CNS by the HRB demonstrated a similar prevalence of abnormality in both groups. Ranch Hands exhibited an increased mean A-H subscore of the CMI, suggesting they had more illness than Comparisons.

12.1.2.3 1987 Follow-up Examination Summary Results

The psychology assessment was based on verified psychological disorders, reported sleep disorders, and two clinical psychological tests, the SCL-90-R and the MCMI, where higher scores may indicate an adverse condition in the psychological health of the participant. Lifetime psychological disorders showed no group differences for psychoses, drug dependence, and anxiety. The Ranch Hands reported experiencing great or disabling fatigue during the day and talking in their sleep more frequently than the Comparisons. After adjusting for the covariates, a significant increase in the Ranch Hand mean was seen on the MCMI narcissistic score. The Comparisons had a significantly higher mean MCMI dependent score than the Ranch Hands.

12.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Examination Summary Results

In general, the results of the analyses of the verified psychological disorders, reported sleep disorders, and the SCL-90-R variables did not reveal significant associations with initial dioxin or 1987 dioxin and time since tour of duty or find significant differences among the four dioxin categories (Comparisons, Ranch

Hands with no more than 10 ppt of 1987 dioxin in the blood, and Ranch Hands with more than 10 ppt of 1987 dioxin in the blood divided into two categories: "Low Ranch Hands" and "High Ranch Hands"). In contrast, several of the analyses of the MCMI variables displayed significant results. There was a lack of consistency across similar variables included in the SCL-90-R, MCMI, and reported information. In conclusion, the body burden of dioxin did not appear to be related to psychological or psychophysiological disorders.

12.1.2.5 1992 Follow-up Examination Summary Results

The psychology assessment was based on verified psychological disorders and the SCL-90-R. Differences in the SCL-90-R inventory variables were found between Ranch Hand and Comparison groups. Variables revealing significant differences in adjusted analyses were other neuroses and the SCL-90-R scores for anxiety, obsessive-compulsive behavior, paranoid ideation, somatization, and the GSI. These differences were observed when combining participants across all occupations. All significant results showed a greater percentage of Ranch Hands than Comparisons that had a history of other neuroses or high (adverse) SCL-90-R scores.

Most of the significant results in the adjusted analysis of the association between the psychological endpoints and categorized dioxin were from the contrasts of Ranch Hands in the background dioxin category with Comparisons. These differences between Ranch Hands in the background dioxin category and Comparisons were found in the analysis of the SCL-90-R obsessive-compulsive behavior, paranoid ideation, and somatization scores. The analysis also revealed that Ranch Hands in the background category had a greater percentage of high SCL-90-R scores than did Comparisons. The adjusted analysis of categorized dioxin also showed a significant increase in the percentage of Ranch Hands in the high dioxin category with a high SCL-90-R anxiety score over Comparisons. In the analyses of 1987 dioxin, a significant inverse association between whole weight 1987 dioxin, adjusted for total lipids, and a history of alcohol dependence was observed.

12.1.2.6 1997 Follow-up Examination Summary Results

Five psychological disorders, which were verified by a medical records review, and 12 measures from the SCL-90-R inventory were examined in the psychology assessment. The SCL-90-R consisted of nine primary symptom dimensions and three broad indices of psychological distress. In enlisted groundcrew, a significantly greater percentage of Ranch Hands than Comparisons had a history of other neuroses. All other adjusted analyses of Ranch Hands versus Comparisons that were significant showed a greater percentage of Comparisons than Ranch Hands with high SCL-90-R scores. High scores on the SCL-90-R may indicate an adverse effect to psychological health.

Associations between initial dioxin and the psychological endpoints in the analyses were either nonsignificant or revealed a significant decrease in high SCL-90-R scores as initial dioxin increased.

Differences in the history of psychological disorders and the prevalence of high SCL-90-R scores were examined between Comparisons and Ranch Hands categorized by dioxin levels. Ranch Hands in the low dioxin category and the low and high dioxin categories combined displayed a significantly higher prevalence of other neuroses than Comparisons.

The relation between the 1987 dioxin levels and the psychological endpoints was examined; all results were nonsignificant.

In conclusion, Ranch Hand veterans exhibited a significantly increased prevalence of other neuroses among enlisted groundcrew, the occupation with the highest dioxin levels and, presumably, the greatest

herbicide exposure. No consistent relation was found between any SCL-90-R score and any measure of herbicide or dioxin exposure.

12.1.3 Parameters for the 2002 Psychology Assessment

12.1.3.1 Dependent Variables

Data collected through the SCL-90-R and the WMS-R were used in the psychology assessment. In addition, psychological disorders, as verified through medical records review, were used to supplement the psychological evaluation for the 2002 follow-up examination. Three Ranch Hands and two Comparisons who tested positive for the human immunodeficiency virus (HIV) were excluded from the analyses of all dependent variables because of the psychological issues associated with initial diagnosis, side effects of anti-viral drug therapy, and the neurocognitive component associated with the disease process.

12.1.3.1.1 Medical Records Variables

At the face-to-face interview during the 2002 examination, each participant was asked whether he had a mental or emotional disorder since the date of his last interview. Medical records review was accomplished to confirm reported mental or emotional disorders and to identify any unreported mental or emotional conditions for each participant that attended the 2002 physical examination. These data from the 2002 physical examination were combined with data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations to form a series of variables regarding a verified history of psychological disorders for each participant. In particular, the verified histories of psychoses (ICD-9-CM codes 290.0–298.9), alcohol dependence (ICD-9-CM codes 303.00–303.93, 303.97–303.98), drug dependence (ICD-9-CM codes 304.00–304.93), anxiety (ICD-9-CM codes 300.00–300.09), and other neuroses (ICD-9-CM codes 300.10–302.9, 305.00–305.03, 305.20-309.9, and 311) were studied. The greatest category of other neuroses resulted from a physiological malfunction arising from mental factors (category name in the ICD-9-CM manual, ICD-9-CM 306). The physiological malfunctions included psychogenic physical symptoms and physiological manifestations. Depressive disorders not elsewhere classified also showed a high prevalence (ICD-9-CM 311). The analyses performed in this chapter were based on the 1,951 participants who attended the 2002 follow-up examination.

In addition to the HIV-positive participants described previously, participants with a verified pre-SEA history of a psychological disorder under study were excluded from the analyses pertaining to that disorder.

12.1.3.1.2 Psychological Examination Variables

The SCL-90-R was used in the psychology assessment for the 2002 follow-up examination, and had been used previously in the AFHS at the 1987, 1992, and 1997 follow-up examinations. The SCL-90-R is a multidimensional self-reported symptom inventory designed to measure symptomatic psychological distress in terms of nine primary symptom dimensions. The nine dimensions are anxiety, depression, hostility, interpersonal sensitivity, obsessive-compulsive behavior, paranoid ideation, phobic anxiety, psychoticism, and somatization. Each participant was asked to respond to 90 questions in terms of the following 5-point scale: 0=not at all, 1=a little bit, 2=moderately, 3=quite a bit, and 4=extremely. High scores on these questions lead to high (adverse) scores for the scales characterizing the nine primary symptom dimensions. Responses were grouped into the nine primary symptom categories, and a raw score for a participant for a category was determined by adding the scores of the answered questions in that category and dividing by the number of answered questions in that category. The raw scores were then converted to T-scores (reference scores for a given population norm) for analysis.

The SCL-90-R also measures distress using three global indices that also were analyzed. The distress indices are the GSI, PST, and PSDI. The GSI is defined as the sum of the scores of all answered questions divided by the number of answered questions on the entire test. This index combines information on the number of symptoms and the intensity of distress. The PST is the number of questions to which the participant responds positively (i.e., on the 5-point scale, responses 1, 2, 3, or 4). The PSDI is determined by adding the scores of all answered questions and dividing by the PST. This index describes the intensity of the positive symptoms. Each of these indices also was converted to a T-score.

The T-scores for the nine primary symptom dimensions and the three global indices were then classified as abnormal or normal, where abnormal was defined as a T-score of 63 or greater. The maximum T-score for AFHS participants attending the 2002 follow-up examination was 81. All participants were included in the analyses of the nine primary symptom dimensions and the three global indices of distress, including those participants who responded "not at all" to all 90 questions.

The WMS-R is an individually administered clinical instrument for appraising major dimensions of memory functions in adolescents and adults. The functions assessed include memory for verbal and figural stimuli, meaningful and abstract material, and delayed as well as immediate recall. The original memory scale was developed by Wechsler in 1945 to permit clinicians in different settings and at different times to assess the same memory functions of their patients. The original WMS was rapid, simple, and practical, but it was limited in its coverage of memory functions believed to be clinically important. The WMS-R modified the content from the original WMS to improve and simplify the scoring system to reduce inter-administrator variability in the grading of the tests. The original WMS was administered for the 1982 AFHS baseline examination and the WMS-R was used for the AFHS 2002 follow-up examination. Three tests of the WMS-R were administered for the AFHS 2002 follow-up examination: the Logical Memory test (immediate and delayed recall), the Verbal Paired Associates test, and the Visual Reproduction test (immediate and delayed recall).

The Logical Memory test includes two brief stories that are read to the participant. After each one, the participant retells the story from memory (immediate recall). Following a delay of 30 minutes, the participant is again asked to relate each story (delayed recall). In the Verbal Paired Associates test, the participant learns eight word pairs, four of which reflect easy associations (e.g., metal – iron) and four of which are more difficult (e.g., crush – dark). For the Visual Reproduction test, the participant is asked to draw from memory four simple geometric designs that are each exposed for 10 seconds (immediate recall). Following a delay of 30 minutes, the participant is again asked to draw each design (delayed recall).

For the Verbal Paired Associates test, four easy associations and four difficult associations are asked three times to each participant. Therefore, a participant could score 12 for the easy items and 12 for the difficult items. In an attempt to mimic the scoring procedure for the WMS, Version 1, which was administered at the baseline examination, a score was constructed by taking the total for the easy items, dividing this score by 2, and adding the total for the difficult items. Therefore, the maximum possible score was 18.

The maximum possible score on each of the two stories read to the participant for the Logical Memory test was 25. An average score across both tests, which were of equal complexity, was used in the analysis in an attempt to mimic the scoring procedure for the WMS, Version 1. Therefore, the maximum possible average was 25. This scoring method was used for both the immediate and delayed recall.

For the Visual Reproduction test, the analysis was based on the sum of the scores from the reproduction of the four geometric figures, as was done for the baseline examination. The maximum possible score was 34. This scoring method was used for both the immediate and delayed recall.

12.1.3.2 Covariates

Covariates to be examined in the adjusted statistical analyses of the psychology assessment included age, race, military occupation, education level (high school, which comprised participants who achieved at most a high school education, and college, which comprised participants who earned a degree beyond high school), current alcohol use (average number of drinks per day during the 2 weeks prior to physical examination), lifetime alcohol history (drink-years), current total household income, current employment (yes, no), current marital status (married, not married), and current parental status (currently having a child under the age of 18 living at home [yes, no]).

Age, race, and military occupation were used as covariates in adjusted statistical analyses evaluating all psychological dependent variables. Age, race, and military occupation were determined from military records. Lifetime alcohol history was based on information from the 2002 questionnaire and combined with similar information gathered at the 1987, 1992, and 1997 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking pattern changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year. Current alcohol use was defined as the average number of drinks per day during the 2 weeks prior to completing the physical examination. These alcohol covariates were not used in adjusted analyses of alcohol dependence.

Current total household income information was collected in the 2002 questionnaire in categories with $5,000 increments, between $5,000 and $100,000. The midpoint of each category was used as the current total household income, with $102,500 used for the $100,000 or more category. Participants who were working full- or part-time were considered to be employed. Those participants who were unemployed, retired, in school, or keeping house were designated as not employed.

Educational level, current employment, current marital status, and current parental status were all based on self-reported information from the questionnaire.

The covariates current total household income, current employment, current marital status, and current parental status were used in the analysis of dependent variables based on medical records data (psychoses, alcohol dependence, drug dependence, anxiety, and other neuroses). Although these dependent variables captured a history of the condition, and the covariates described above were based on the current status of a participant's life, the covariates were used as surrogate information to describe the participant's life experience. In addition, lifetime alcohol history was used as a covariate for these dependent variables, but current alcohol use was not used. Current alcohol use reflected a participant's alcohol use only in the 2 weeks prior to the physical examination. The lifetime alcohol history covariate was used to investigate the cumulative lifetime effects of alcohol use.

12.1.4 Statistical Methods

Table 12-1 summarizes the statistical analysis performed for the 2002 psychology assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, exclusions, and statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to

develop measures of association with the dependent variables, the covariate was categorized as shown in Table 12-1.

Table 12-1. Statistical Analysis for the Psychology Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Psychoses	MR-V	D	Present Absent	(1)	(a)	U:LR,CS A:LR
Alcohol Dependence	MR-V	D	Present Absent	(2)	(a)	U:LR,CS A:LR
Drug Dependence	MR-V	D	Present Absent	(1)	(a)	U:LR,CS A:LR
Anxiety	MR-V	D	Present Absent	(1)	(a)	U:LR,CS A:LR
Other Neuroses	MR-V	D	Present Absent	(1)	(a)	U:LR,CS A:LR
SCL-90-R Anxiety	PE	D	Abnormal: T≥63 Normal: T<63	(3)	(b)	U:LR,CS A:LR
SCL-90-R Depression	PE	D	Abnormal: T≥63 Normal: T<63	(3)	(b)	U:LR,CS A:LR
SCL-90-R Hostility	PE	D	Abnormal: T≥63 Normal: T<63	(3)	(b)	U:LR,CS A:LR
SCL-90-R Interpersonal Sensitivity	PE	D	Abnormal: T≥63 Normal: T<63	(3)	(b)	U:LR,CS A:LR
SCL-90-R Obsessive-compulsive Behavior	PE	D	Abnormal: T≥63 Normal: T<63	(3)	(b)	U:LR,CS A:LR
SCL-90-R Paranoid Ideation	PE	D	Abnormal: T≥63 Normal: T<63	(3)	(b)	U:LR,CS A:LR
SCL-90-R Phobic Anxiety	PE	D	Abnormal: T≥63 Normal: T<63	(3)	(b)	U:LR,CS A:LR
SCL-90-R Psychoticism	PE	D	Abnormal: T≥63 Normal: T<63	(3)	(b)	U:LR,CS A:LR
SCL-90-R Somatization	PE	D	Abnormal: T≥63 Normal: T<63	(3)	(b)	U:LR,CS A:LR
SCL-90-R GSI	PE	D	Abnormal: T≥63 Normal: T<63	(3)	(b)	U:LR,CS A:LR
SCL-90-R PST	PE	D	Abnormal: T≥63 Normal: T<63	(3)	(b)	U:LR,CS A:LR
SCL-90-R PSDI	PE	D	Abnormal: T≥63 Normal: T<63	(3)	(b)	U:LR,CS A:LR
WMS-R: Verbal Paired Associates	PE	C	--	(3)	(b)	U:GLM,TT A:GLM

Table 12-1. Statistical Analysis for the Psychology Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
WMS-R: Logical Memory, Immediate Recall	PE	C	--	(3)	(b)	U:GLM,TT A:GLM
WMS-R: Logical Memory, Delayed Recall	PE	C	--	(3)	(b)	U:GLM,TT A:GLM
WMS-R: Visual Reproduction, Immediate Recall	PE	C	--	(3)	(b)	U:GLM,TT A:GLM
WMS-R: Visual Reproduction, Delayed Recall	PE	C	--	(3)	(b)	U:GLM,TT A:GLM

[a]Covariates:

(1) age, race, military occupation, education, lifetime alcohol history, current total household income, current employment, current marital status, current parental status.

(2) age, race, military occupation, education, current total household income, current employment, current marital status, current parental status.

(3) age, race, military occupation, education, current alcohol use, lifetime alcohol history, current total household income, current employment, current marital status, current parental status.

[b]Exclusions:

(a) participants with a pre-SEA history of the disorder, participants testing positive for HIV.

(b) participants testing positive for HIV.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	C/D	Born ≥ 1942 Born < 1942
Race	MIL	D	Black Non-Black
Military Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Education	Q-SR	D	College High School
Current Alcohol Use (2 weeks prior to physical exam) (drinks/day)	Q-SR	C/D	0–1 >1
Lifetime Alcohol History (drink-years)	Q-SR	C/D	0 >0–40 >40
Current Total Household Income (dollars)	Q-SR	C/D	<$65,000 ≥$65,000
Current Employment	Q-SR	D	Yes No
Current Marital Status	Q-SR	D	Married Not Married
Current Parental Status	Q-SR	D	Child <18 years old living at home No child <18 years old living at home

Abbreviations

Data Source: MIL: Air Force military records
MR-V: Medical records (verified)
PE: 2002 psychological examination
Q-SR: Health questionnaires (self-reported)

Data Form: C: Continuous form of dependent variable
D: Discrete form of dependent variable or covariate
C/D: Appropriate form for analysis (either continuous or discrete) of covariate

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
LR: Logistic regression analysis
GLM: General linear models analysis
TT: Two-sample t-test

Four models were examined for each dependent variable given in Table 12-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for covariates. These covariates are given in Table 12-1. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. In an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-4, the median level of exposure to dioxin was highest for enlisted groundcrew, followed by enlisted flyers, then officers.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the CDC using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in ppt on a lipid weight basis (53). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2. A statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model to account for body mass index-related differences in elimination rate (54).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were

formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. Another category was examined by combining the low and high Ranch Hand categories. This combination is referred to in the tables as the "low plus high Ranch Hand" category. These five categories—Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the four Ranch Hand categories and the dependent variable in the Comparison category was examined. As in Model 2, a statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables. One Ranch Hand without a dioxin measure was excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The term "unadjusted" was used in the text and tables as follows: Models 1 and 4 did not adjust for any covariates. Models 2 and 3 adjusted only for body mass index at the time of the blood measurement for dioxin. The term "adjusted" was used in the text and tables as follows: Models 1 and 4 adjusted for the covariates shown in Table 12-1 unless otherwise specified by a footnote to the table. Models 2 and 3 additionally adjusted only for body mass index at the time of the blood measurement for dioxin.

Table 12-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants that were excluded from analyses is given. As noted in Table 12-2, 55 participants did not provide information for current total household income. Most of these participants refused to answer this question. In an attempt not to exclude a substantial number of participants, a limited version of a stepwise procedure was used. If current total household income was not significant ($p > 0.05$) for the adjusted analysis of a particular model for a dependent variable, this covariate was excluded from the analysis. Excluding current total household income from the model allowed these 55 participants to be included in the analysis of the model and thus increased the sample size. The parameters of the model were then re-estimated; these statistics are shown in the tables in this chapter. Those models for which current total household income was deleted as a covariate are noted in a footnote to the table.

Table 12-2. Number of Participants Excluded or with Missing Data for the Psychology Assessment

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
SCL-90-R Categories and Indices	DEP	2	1	1	2	2	1
WMS-R Verbal Associates	DEP	1	3	0	1	1	3
WMS-R: Logical Memory, Immediate Recall	DEP	1	3	0	1	1	3
WMS-R: Logical Memory, Delayed Recall	DEP	1	4	0	1	1	4
WMS-R: Visual Reproduction, Immediate Recall	DEP	1	5	0	1	1	5
WMS-R: Visual Reproduction, Delayed Recall	DEP	1	5	0	1	1	5
Education	COV	0	2	0	0	0	2
Current Alcohol Use	COV	0	2	0	0	0	2
Lifetime Alcohol History	COV	4	5	3	4	4	5
Current Total Household Income	COV	20	35	12	20	20	35
Current Employment	COV	1	2	1	1	1	2
Current Marital Status	COV	0	3	0	0	0	3
Current Parental Status	COV	0	2	0	0	0	2
Pre-SEA Alcohol Dependence	EXC	0	1	0	0	0	1
Pre-SEA Anxiety	EXC	3	3	1	3	3	3
Pre-SEA Other Neuroses	EXC	8	10	2	8	8	10
HIV Positive	EXC	3	2	3	3	3	2

[a]777 Ranch Hands and 1,174 Comparisons for group.
[b]424 Ranch Hands for initial dioxin; 776 Ranch Hands for 1987 dioxin.
[c]776 Ranch Hands and 1,174 Comparisons for categorized dioxin.

Note: DEP = Dependent variable.
    COV = Covariate.
    EXC = Exclusion.

12.2   RESULTS

12.2.1   Dependent Variable-covariate Associations

The psychological dependent variables were tested for associations with each of the covariates used in the adjusted analyses. The complete results are presented in Appendix F, Table F-4. These associations were pairwise between the dependent variable and the covariate and were not adjusted for any other covariates. The following paragraphs provide a brief summary of the pattern of significant ($p \leq 0.05$) dependent variable-covariate associations. In the discussion of the results below, low levels are considered adverse for the WMS-R test scores.

Age was significantly associated with a history of anxiety, as verified by a medical records review. Age was also associated with all WMS-R tests conducted. The SCL-90-R subscales of anxiety, hostility, interpersonal sensitivity, paranoid ideation, phobic anxiety, GSI, and PST showed a significant association with age. Scores on the WMS-R were greater for younger participants. A greater percentage of younger participants had a history of anxiety or high SCL-90-R scores than did older participants.

Black participants had a significantly higher history of psychoses, as verified by a medical records review, than did non-Black participants. The same pattern was observed for the SCL-90-R subscales of anxiety, interpersonal sensitivity, paranoid ideation, phobic anxiety, psychoticism, GSI, and PST. Non-Black participants scored higher on both the immediate and delayed recall portions of the Logical Memory and Visual Reproduction WMS-R tests.

All dependent variables were significantly associated with military occupation, except for drug dependence. Officers consistently had the smallest percentage of abnormal results and the highest scores on the WMS-R memory tests. Enlisted groundcrew had the greatest percentage of abnormalities on the variables derived from medical records and on the majority of SCL-90-R subscales. Enlisted flyers had the lowest average score on all WMS-R tests. These significant results may be related to the strong relation between education and occupation, as noted for the 1982 baseline examination and observed in all subsequent follow-up examinations. Many of the participants with at most a high-school education were enlisted personnel, whereas the majority of college-educated participants were officers.

Participants with at most a high school education had significantly higher prevalences of psychoses, anxiety, and other neuroses. Participants with college degrees had lower prevalences of abnormally high scores on all SCL-90-R subscales and higher average scores on all WMS-R tests.

Current alcohol use was significantly associated with the delayed and immediate recall portions of the Logical Memory and Visual Reproduction WMS-R tests. Scores on these memory tests increased as current alcohol use increased. These significant associations were probably due to the associations between military occupation and the memory tests and between military occupation and current alcohol use. Officers were heavier current drinkers than enlisted personnel, and officers also scored higher on the memory tests.

Lifetime alcohol history was significantly associated with a history of psychoses and other neuroses and the WMS-R Visual Reproduction (both delayed and immediate) tests. The SCL-90-R subscales of depression, hostility, obsessive-compulsive behavior, paranoid ideation, psychoticism, GSI, and PST also showed significant associations with lifetime alcohol history. In most cases, the heaviest lifetime drinkers (in terms of drink-years) had the greatest percentage of abnormalities on the variables derived from medical records or high SCL-90-R subscale scores. As lifetime alcohol consumption increased, the scores on the Visual Reproduction tests decreased.

All dependent variables were significantly associated with current total household income, except for drug dependence. Participants who had a higher income displayed a smaller prevalence of abnormalities. In addition, as income increased, the scores on the WMS-R memory tests increased.

Current employment was significantly associated with a history of psychoses, other neuroses, and all SCL-90-R and WMS-R tests. Participants who were currently employed had a smaller percentage of abnormalities and higher scores on the WMS-R memory tests than participants who were not currently employed.

Current marital status was significantly associated with all variables verified by a medical records review. With the exception of hostility, somatization, and the PSDI, current marital status was significantly associated with the SCL-90-R dependent variables. Participants who were not currently married had a greater percentage of abnormal scores. Participants who were currently married had higher average scores on the delayed recall portion of the WMS-R Logical Memory test and the immediate and delayed recall portions of the Visual Reproduction test.

Participants who currently had a child less than 18 years of age living at home had a greater prevalence of a history of other neuroses than participants who did not. In addition, the participants who had a child less than 18 years of age living at home scored higher, on average, on the immediate and delayed recall portions of the WMS-R Visual Reproduction test.

12.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 12-1. Dependent variables are grouped into two sections: (1) the questionnaire variables, derived from the questionnaire that was administered in the 2002 follow-up and previous AFHS examinations, and (2) the psychological examination variables, obtained during the 2002 physical examination.

12.2.2.1 Medical Records Variables

12.2.2.1.1 Psychoses

All results from the unadjusted and adjusted analyses of a history of psychoses (Models 1 through 4) were nonsignificant (Table 12-3(a-h): $p>0.20$ for each analysis).

Table 12-3. Analysis of Psychoses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*774*	*46 (5.9)*	*0.94 (0.64,1.37)*	*0.739*
	Comparison	*1,172*	*74 (6.3)*		
Officer	Ranch Hand	307	8 (2.6)	0.80 (0.33,1.90)	0.607
	Comparison	461	15 (3.3)		
Enlisted Flyer	Ranch Hand	133	13 (9.8)	1.56 (0.69,3.54)	0.286
	Comparison	185	12 (6.5)		
Enlisted Groundcrew	Ranch Hand	334	25 (7.5)	0.82 (0.50,1.37)	0.455
	Comparison	526	47 (8.9)		

Table 12-3. Analysis of Psychoses (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,885*	*0.97 (0.65,1.44)*	*0.876*
Officer	749	0.77 (0.32,1.85)	0.562
Enlisted Flyer	305	1.73 (0.74,4.06)	0.208
Enlisted Groundcrew	831	0.85 (0.50,1.43)	0.538

Note: Current total household income was not included in the model (see Section 12.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	10 (7.1)	1.05 (0.79,1.40)	0.719
Medium	143	9 (6.3)		
High	138	9 (6.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	0.94 (0.68,1.31)	0.715

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

Table 12-3. Analysis of Psychoses (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	74 (6.3)		
Background RH	352	18 (5.1)	0.81 (0.48,1.38)	0.436
Low RH	211	12 (5.7)	0.89 (0.48,1.67)	0.721
High RH	210	16 (7.6)	1.21 (0.69,2.13)	0.506
Low plus High RH	421	28 (6.7)	1.04 (0.66,1.64)	0.870

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	351	1.03 (0.59,1.80)	0.927
Low RH	210	1.01 (0.53,1.94)	0.970
High RH	207	0.89 (0.49,1.62)	0.707
Low plus High RH	417	0.95 (0.59,1.52)	0.834

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

    Current total household income was not included in the model (see Section 12.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	12 (4.6)	1.10 (0.92,1.33)	0.291
Medium	258	17 (6.6)		
High	255	17 (6.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 12-3. Analysis of Psychoses (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
768	0.97 (0.80,1.17)	0.732

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.1.2 Alcohol Dependence

Analysis of a history of alcohol dependence revealed nonsignificant results for each unadjusted and adjusted analysis (Models 1 through 4) (Table 12-4(a-h): p≥0.18 for each analysis).

Table 12-4. Analysis of Alcohol Dependence

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*774*	*46 (5.9)*	*1.06 (0.72,1.56)*	*0.776*
	Comparison	*1,171*	*66 (5.6)*		
Officer	Ranch Hand	307	10 (3.3)	0.71 (0.33,1.52)	0.373
	Comparison	461	21 (4.6)		
Enlisted Flyer	Ranch Hand	133	8 (6.0)	0.85 (0.34,2.10)	0.720
	Comparison	185	13 (7.0)		
Enlisted Groundcrew	Ranch Hand	334	28 (8.4)	1.41 (0.83,2.39)	0.201
	Comparison	525	32 (6.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,890*	*1.06 (0.71,1.59)*	*0.774*
Officer	749	0.68 (0.30,1.52)	0.350
Enlisted Flyer	308	0.84 (0.33,2.14)	0.716
Enlisted Groundcrew	833	1.43 (0.83,2.47)	0.196

Table 12-4. Analysis of Alcohol Dependence (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	7 (5.0)	1.08 (0.80,1.47)	0.626
Medium	143	6 (4.2)		
High	138	11 (8.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
420	1.01 (0.71,1.43)	0.961

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	66 (5.6)		
Background RH	352	22 (6.3)	1.09 (0.66,1.79)	0.748
Low RH	211	10 (4.7)	0.84 (0.42,1.66)	0.613
High RH	210	14 (6.7)	1.23 (0.67,2.23)	0.505
Low plus High RH	421	24 (5.7)	1.01 (0.62,1.65)	0.957

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 12-4. Analysis of Alcohol Dependence (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,136		
Background RH	344	1.28 (0.76,2.16)	0.357
Low RH	202	0.84 (0.41,1.74)	0.638
High RH	207	0.95 (0.50,1.80)	0.875
Low plus High RH	409	0.89 (0.53,1.50)	0.670

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	15 (5.8)	1.00 (0.83,1.20)	0.997
Medium	258	15 (5.8)		
High	255	16 (6.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
772	0.87 (0.72,1.06)	0.180

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.1.3 Drug Dependence

Due to a small prevalence of participants with a verified history of drug dependence, only limited analyses of drug dependence were possible. All results from unadjusted and adjusted analyses performed for Models 1, 3, and 4 were nonsignificant (Table 12-5(a,b,e-h): p>0.17 for each analysis). No Ranch Hands in the Model 2 analyses had a history of drug dependence and analysis was not possible.

Table 12-5. Analysis of Drug Dependence

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*774*	*2 (0.3)*	*0.60 (0.12,3.12)*	0.535
	Comparison	*1,172*	*5 (0.4)*		
Officer	Ranch Hand	307	0 (0.0)	--	0.999[a]
	Comparison	461	1 (0.2)		
Enlisted Flyer	Ranch Hand	133	0 (0.0)	--	--
	Comparison	185	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	334	2 (0.6)	0.79 (0.14,4.32)	0.782
	Comparison	526	4 (0.8)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with drug dependence present.

--: Results were not presented because of the sparse number of Ranch Hands with drug dependence present.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,885*	*0.67 (0.12,3.77)*	*0.647*
Officer	749	--	--
Enlisted Flyer	305	--	--
Enlisted Groundcrew	831	0.89 (0.15,5.40)	0.899

--: Results were not presented because of the sparse number of participants with drug dependence present.

Note: Results were not adjusted for military occupation because of the sparse number of participants with drug dependence present.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
Low	140	0 (0.0)	--	--
Medium	143	0 (0.0)		
High	138	0 (0.0)		

--: Results were not presented because no Ranch Hands have a drug dependence.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 12-5. Analysis of Drug Dependence (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)**	**p-Value**
406	--	--

--: Results were not presented because no Ranch Hands have a drug dependence.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,172	5 (0.4)		
Background RH	352	2 (0.6)	0.99 (0.19,5.19)	0.990
Low RH	211	0 (0.0)	--	0.743[c]
High RH	210	0 (0.0)	--	0.746[c]
Low plus High RH	421	0 (0.0)	--	0.404[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with drug dependence present.

--: Results were not presented because of the sparse number of Ranch Hands with drug dependence present.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,166		
Background RH	351	0.88 (0.14,5.61)	0.892
Low RH	210	--	--
High RH	207	--	--
Low plus High RH	417	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of Ranch Hands with drug dependence present.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for military occupation and current total household income because of the sparse number of participants with drug dependence present.

Table 12-5. Analysis of Drug Dependence (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	2 (0.8)	0.54 (0.23,1.29)	0.178
Medium	258	0 (0.0)		
High	255	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	0.51 (0.16,1.61)	0.224

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, military occupation, current total household income, current employment, current marital status, and current parental status because of the sparse number of Ranch Hands with drug dependence present.

12.2.2.1.4 *Anxiety*

All Model 1 through Model 3 results were nonsignificant for the unadjusted and adjusted analyses of anxiety (Table 12-6(a-f): p>0.05 for each analysis). A significant positive association between 1987 dioxin levels and the prevalence of a history of anxiety was found in the unadjusted Model 4 analysis (Table 12-6(g): p=0.003, Unadjusted Relative Risk [RR]=1.16). The Model 4 result was nonsignificant after adjusting for covariates (Table 12-6(h): p=0.547).

Table 12-6. Analysis of Anxiety

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*226 (29.3)*	*1.05 (0.86,1.28)*	*0.635*
	Comparison	*1,169*	*331 (28.3)*		
Officer	Ranch Hand	307	50 (16.3)	0.80 (0.55,1.17)	0.256
	Comparison	461	90 (19.5)		
Enlisted Flyer	Ranch Hand	132	44 (33.3)	1.07 (0.66,1.72)	0.787
	Comparison	185	59 (31.9)		
Enlisted Groundcrew	Ranch Hand	332	132 (39.8)	1.24 (0.93,1.64)	0.143
	Comparison	523	182 (34.8)		

Table 12-6. Analysis of Anxiety (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,879*	*1.06 (0.86,1.30)*	*0.598*
Officer	749	0.83 (0.56,1.22)	0.336
Enlisted Flyer	304	1.09 (0.67,1.78)	0.735
Enlisted Groundcrew	826	1.21 (0.90,1.62)	0.201

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	37 (26.4)	1.13 (0.97,1.31)	0.128
Medium	143	51 (35.7)		
High	137	48 (35.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	0.94 (0.78,1.13)	0.497

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

Table 12-6. Analysis of Anxiety (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,169	331 (28.3)		
Background RH	350	89 (25.4)	0.87 (0.66,1.14)	0.314
Low RH	211	63 (29.9)	1.08 (0.78,1.48)	0.656
High RH	209	73 (34.9)	1.35 (0.99,1.85)	0.059
Low plus High RH	420	136 (32.4)	1.21 (0.95,1.53)	0.131

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,132		
Background RH	341	1.07 (0.80,1.43)	0.666
Low RH	201	1.17 (0.83,1.63)	0.374
High RH	204	0.95 (0.68,1.32)	0.767
Low plus High RH	405	1.05 (0.82,1.35)	0.693

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	258	60 (23.3)	1.16 (1.05,1.28)	0.003**
Medium	258	74 (28.7)		
High	254	91 (35.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value$\leq$0.010).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 12-6. Analysis of Anxiety (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log_2 (1987 Dioxin) | |
| | **Adjusted Relative Risk** | |
n	**(95% C.I.)[a]**	**p-Value**
765	0.97 (0.87,1.08)	0.547

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.1.5 Other Neuroses

Model 1 unadjusted and adjusted analyses of other neuroses revealed a significant difference between Ranch Hands and Comparisons within the officer stratum (Table 12-7(a,b): p=0.029, Unadjusted RR=0.72; and p=0.043, Adjusted RR=0.73, respectively). The percentages of Comparison and Ranch Hand officers who had a verified history of other neuroses were 51.5 and 43.5, respectively. All other Model 1 contrasts were nonsignificant, as was each result from the Model 2 unadjusted and adjusted analyses (Table 12-7(a-d): p>0.06 for each result).

Several significant contrasts were found in the Model 3 unadjusted analysis of other neuroses (Table 12-7(e): p=0.020, Unadjusted RR=0.75, for Ranch Hands in the background dioxin category versus Comparisons; p=0.028, Unadjusted RR=1.43, for Ranch Hands in the high dioxin category versus Comparisons; and p=0.048, Unadjusted RR=1.27, for Ranch Hands in the low and high dioxin categories combined versus Comparisons). The percentage of participants with a verified history of other neuroses was higher for Comparisons (59.6%) than Ranch Hands in the background dioxin category (51.7%), but lower for Comparisons than for Ranch Hands in both the high dioxin category and low and high dioxin categories combined (68.3% and 65.4%, respectively). The remaining Model 3 unadjusted contrast was nonsignificant, as was each contrast in the adjusted Model 3 analysis (Table 12-7(f): p>0.35 for each contrast).

A significant positive association between 1987 dioxin levels and other neuroses was found within the Model 4 unadjusted analysis (Table 12-7(g): p<0.001, Unadjusted RR=1.19). After adjusting for covariates, the association was nonsignificant (Table 12-7(h): p=0.819).

Table 12-7. Analysis of Other Neuroses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*454 (59.3)*	*0.99 (0.82,1.19)*	*0.901*
	Comparison	*1,162*	*692 (59.6)*		
Officer	Ranch Hand	306	133 (43.5)	0.72 (0.54,0.97)	0.029*
	Comparison	458	236 (51.5)		
Enlisted Flyer	Ranch Hand	132	92 (69.7)	1.15 (0.71,1.86)	0.570
	Comparison	183	122 (66.7)		
Enlisted Groundcrew	Ranch Hand	328	229 (69.8)	1.30 (0.96,1.74)	0.087
	Comparison	521	334 (64.1)		

*: Statistically significant (0.01<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,867*	*1.01 (0.83,1.23)*	*0.901*
Officer	745	0.73 (0.54,0.99)	0.043*
Enlisted Flyer	302	1.19 (0.72,1.97)	0.491
Enlisted Groundcrew	820	1.34 (0.98,1.82)	0.067

*: Statistically significant (0.01<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	80 (57.1)	1.07 (0.92,1.25)	0.369
Medium	143	102 (71.3)		
High	136	92 (67.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 12-7. Analysis of Other Neuroses (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
415	0.95 (0.79,1.16)	0.626

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,162	692 (59.6)		
Background RH	346	179 (51.7)	0.75 (0.59,0.95)	0.020*
Low RH	211	132 (62.6)	1.13 (0.83,1.53)	0.439
High RH	208	142 (68.3)	1.43 (1.04,1.96)	0.028*
Low plus High RH	419	274 (65.4)	1.27 (1.00,1.60)	0.048*

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.01 < $p-value$ \leq 0.050$).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,125		
Background RH	337	0.90 (0.69,1.17)	0.442
Low RH	201	1.14 (0.83,1.57)	0.416
High RH	203	1.11 (0.79,1.56)	0.552
Low plus High RH	404	1.13 (0.88,1.44)	0.353

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 12-7. Analysis of Other Neuroses (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Present**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	255	126 (49.4)	1.19 (1.09,1.31)	<0.001**
Medium	257	151 (58.8)		
High	253	176 (69.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
760	1.01 (0.90,1.14)	0.819

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2 Psychological Examination Variables

The 12 variables contained in this section are derived from the SCL-90-R. These 12 variables comprise primary symptom categories and three global indices of distress. A short description, which has been taken from the SCL-90-R reference manual (1), of each of the primary symptom categories and global indices of distress is given before the description of the results of the statistical analyses. The function of each of these global measures of the SCL-90-R, the GSI, the PSDI, and the PST, is to communicate in a single score the level or depth of the individual's psychopathology.

Seven items are part of the SCL-90-R, but not part of any of the primary symptom dimensions. These seven items, which influence several of the dimensions but are not unique to any of them, are a poor appetite, overeating, trouble falling asleep, awakening in the early morning, restless or disturbed sleep, thinking of death or dying, and feeling guilty. While in this sense they violate one of the statistical criteria for inclusion in the test, they are a part of the item set because they are clinically important. These items contribute to the global scores on the SCL-90-R and are intended to be used to give additional understanding of the clinical significance of the primary symptom dimensions. Thus, a high depression score with "early morning awakening" and "poor appetite" may mean something quite different from a similar score with these symptoms absent. By the same token, the presence of conscious "feelings of guilt" is an important clinical indicator that communicates important information to the clinician. The additional items are not scored collectively as a dimension but are summed into the global scores.

12.2.2.2.1 SCL-90-R Anxiety

The anxiety dimension is a set of signs and symptoms that are associated clinically with high levels of manifest anxiety. General signs such as nervousness, tension, and trembling are included in the definition, as are panic attacks and feelings of terror. Cognitive components involving feelings of apprehension and dread, and some of the somatic correlates of anxiety, also are included as dimensional components. The symptoms comprising the anxiety dimension are experiencing nervousness or shakiness inside, trembling, being suddenly scared for no reason, feeling fearful, experiencing heart pounding or racing, feeling tense and keyed up, having spells of terror and panic, feeling so restless you couldn't sit still, feeling that something bad is going to happen, and experiencing frightening thoughts and images.

Unadjusted and adjusted analysis results for SCL-90-R anxiety were nonsignificant for Model 1 through Model 3 (Table 12-8(a-f): p>0.05 for each analysis).

The unadjusted analysis of Model 4 revealed a significant positive association between the 1987 dioxin levels and the prevalence of high SCL-90-R anxiety scores (Table 12-8(g): p=0.047, Unadjusted RR=1.17). After covariate adjustment, the association was nonsignificant (Table 12-8(h): p=0.443).

Table 12-8. Analysis of SCL-90-R Anxiety

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*65*	*(8.4)*	*0.92 (0.67,1.28)*	*0.629*
	Comparison	*1,171*	*106*	*(9.1)*		
Officer	Ranch Hand	307	8	(2.6)	0.56 (0.25,1.28)	0.170
	Comparison	461	21	(4.6)		
Enlisted Flyer	Ranch Hand	133	12	(9.0)	0.82 (0.39,1.74)	0.602
	Comparison	185	20	(10.8)		
Enlisted Groundcrew	Ranch Hand	332	45	(13.6)	1.11 (0.74,1.67)	0.617
	Comparison	525	65	(12.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,884*	*0.88 (0.63,1.24)*	*0.459*
Officer	749	0.58 (0.25,1.33)	0.196
Enlisted Flyer	305	0.83 (0.38,1.81)	0.640
Enlisted Groundcrew	830	1.01 (0.66,1.55)	0.964

Table 12-8. Analysis of SCL-90-R Anxiety (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Abnormal**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	140	14 (10.0)	1.00 (0.79,1.26)	0.997
Medium	142	17 (12.0)		
High	138	13 (9.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
416	0.80 (0.60,1.06)	0.115

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	106 (9.1)		
Background RH	351	20 (5.7)	0.62 (0.38,1.01)	0.056
Low RH	210	19 (9.0)	0.99 (0.60,1.66)	0.983
High RH	210	25 (11.9)	1.34 (0.84,2.13)	0.220
Low plus High RH	420	44 (10.5)	1.15 (0.79,1.68)	0.454

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 12-8. Analysis of SCL-90-R Anxiety (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	0.76 (0.45,1.29)	0.312
Low RH	201	1.01 (0.58,1.75)	0.976
High RH	205	0.87 (0.53,1.44)	0.594
Low plus High RH	406	0.94 (0.63,1.40)	0.751

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	15 (5.8)	1.17 (1.00,1.37)	0.047*
Medium	258	20 (7.8)		
High	254	29 (11.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.01<p-value$\leq$0.050).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
766	0.94 (0.79,1.11)	0.443

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.2 SCL-90-R Depression

The symptoms of the depression dimension reflect a broad range of the manifestations of clinical depression. Symptoms of dysphoric mood and affect are represented, as are signs of withdrawal of life interest, lack of motivation, and loss of vital energy. In addition, feelings of hopelessness, thoughts of suicide, and other cognitive and somatic correlates of depression are included. The symptoms comprising

the depression dimension are losing sexual interest or pleasure, feeling low in energy or slowed down, thinking of ending your life, crying easily, feeling trapped or caught, blaming yourself for things, feeling lonely, feeling blue, worrying too much about things, feeling no interest in things, feeling hopeless about the future, feeling everything is an effort, and feeling worthless.

All results from the analysis of SCL-90-R depression (Model 1 through Model 4) were nonsignificant, both unadjusted and adjusted for covariates (Table 12-9(a-h): $p > 0.07$ for each analysis).

Table 12-9. Analysis of SCL-90-R Depression

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*85 (11.0)*	*0.89 (0.67,1.18)*	*0.419*
	Comparison	*1,171*	*143 (12.2)*		
Officer	Ranch Hand	307	19 (6.2)	0.73 (0.42,1.30)	0.289
	Comparison	461	38 (8.2)		
Enlisted Flyer	Ranch Hand	133	13 (9.8)	0.80 (0.39,1.66)	0.552
	Comparison	185	22 (11.9)		
Enlisted Groundcrew	Ranch Hand	332	53 (16.0)	1.01 (0.69,1.47)	0.952
	Comparison	525	83 (15.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,884*	*0.85 (0.63,1.15)*	*0.285*
Officer	749	0.74 (0.41,1.31)	0.298
Enlisted Flyer	305	0.76 (0.36,1.60)	0.469
Enlisted Groundcrew	830	0.94 (0.63,1.40)	0.764

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

	Initial Dioxin Category Summary Statistics		Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	16 (11.4)	1.05 (0.85,1.29)	0.673
Medium	142	19 (13.4)		
High	138	19 (13.8)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 12-9. Analysis of SCL-90-R Depression (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
416	0.95 (0.73,1.24)	0.713

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	143 (12.2)		
Background RH	351	31 (8.8)	0.73 (0.48,1.09)	0.126
Low RH	210	21 (10.0)	0.79 (0.49,1.28)	0.335
High RH	210	33 (15.7)	1.29 (0.85,1.95)	0.225
Low plus High RH	420	54 (12.9)	1.01 (0.72,1.42)	0.960

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	0.80 (0.52,1.23)	0.302
Low RH	201	0.83 (0.50,1.37)	0.461
High RH	205	0.94 (0.60,1.47)	0.797
Low plus High RH	406	0.88 (0.62,1.27)	0.499

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 12-9. Analysis of SCL-90-R Depression (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	19 (7.3)	1.13 (0.99,1.30)	0.076
Medium	258	29 (11.2)		
High	254	37 (14.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
766	0.97 (0.84,1.14)	0.744

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.3 SCL-90-R Hostility

The hostility dimension reflects thoughts, feelings, or actions that are characteristic expressions of anger. The items comprising the hostility dimension were selected to measure the three modes of manifestation (i.e., thoughts, feelings, actions) and reflect qualities such as aggression, irritability, rage, and resentment. The dimension's symptoms are feeling easily annoyed or irritated; having uncontrollable temper outbursts; having urges to beat, injure, or harm someone; having urges to break or smash things; getting into frequent arguments; and shouting or throwing things.

No significant results were found from all unadjusted and adjusted analyses of SCL-90-R hostility for Model 1 through Model 4 (Table 12-10(a-h): p≥0.06 for each analysis).

Table 12-10. Analysis of SCL-90-R Hostility

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*41 (5.3)*	*0.95 (0.64,1.43)*	*0.819*
	Comparison	*1,171*	*65 (5.6)*		
Officer	Ranch Hand	307	4 (1.3)	0.49 (0.16,1.55)	0.226
	Comparison	461	12 (2.6)		
Enlisted Flyer	Ranch Hand	133	8 (6.0)	0.68 (0.28,1.63)	0.383
	Comparison	185	16 (8.6)		
Enlisted Groundcrew	Ranch Hand	332	29 (8.7)	1.26 (0.76,2.10)	0.368
	Comparison	525	37 (7.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,884*	*0.96 (0.63,1.45)*	*0.839*
Officer	749	0.48 (0.15,1.51)	0.210
Enlisted Flyer	305	0.66 (0.27,1.64)	0.370
Enlisted Groundcrew	830	1.29 (0.76,2.18)	0.339

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	4 (2.9)	1.31 (0.98,1.74)	0.077
Medium	142	10 (7.0)		
High	138	10 (7.2)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.09 (0.76,1.56)	0.646

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

Table 12-10. Analysis of SCL-90-R Hostility (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	65 (5.6)		
Background RH	351	17 (4.8)	0.89 (0.51,1.54)	0.664
Low RH	210	5 (2.4)	0.41 (0.16,1.04)	0.060
High RH	210	19 (9.0)	1.66 (0.97,2.84)	0.064
Low plus High RH	420	24 (5.7)	0.83 (0.47,1.45)	0.509

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	1.12 (0.62,2.00)	0.710
Low RH	201	0.46 (0.18,1.19)	0.110
High RH	205	1.15 (0.65,2.02)	0.634
Low plus High RH	406	0.73 (0.41,1.30)	0.289

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	12 (4.6)	1.18 (0.97,1.42)	0.097
Medium	258	9 (3.5)		
High	254	20 (7.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 12-10. Analysis of SCL-90-R Hostility (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
748	0.94 (0.77,1.15)	0.548

[a]Relative risk for a twofold increase in 1987 dioxin.

12.2.2.2.4 SCL-90-R Interpersonal Sensitivity

The interpersonal sensitivity dimension focuses on feelings of personal inadequacy and inferiority, particularly in comparison with others. Self-deprecation, feelings of uneasiness, and marked discomfort during interpersonal interactions are characteristic manifestations of interpersonal sensitivity. In addition, individuals with high scores on interpersonal sensitivity report acute self-consciousness and negative expectations concerning the communications and interpersonal behaviors with others. The symptoms comprising the interpersonal sensitivity dimension are feeling critical of others, feeling shy or uneasy with the opposite sex, having feelings easily hurt, feeling others do not understand or are unsympathetic to, feeling that people are unfriendly or dislike you, feeling inferior to others, feeling uneasy when people are watching or talking about you, feeling very self-conscious with others, and feeling uncomfortable about eating or drinking in public.

Significant differences between Ranch Hands and Comparisons were revealed in the Model 1 unadjusted analysis of SCL-90-R interpersonal sensitivity when examined across all occupational strata and within the officer stratum (Table 12-11(a): p=0.014, Unadjusted RR=0.67; and p=0.040, Unadjusted RR=0.47, respectively). Both contrasts revealed more Comparisons than Ranch Hands with high SCL-90-R interpersonal sensitivity scores (Table 12-11(a): overall: 10.7% for Comparisons versus 7.4% for Ranch Hands; and officer: 6.7% for Comparisons versus 3.3% for Ranch Hands). Results remained significant after adjusting for covariates (Table 12-11(b): p=0.013, Adjusted RR=0.65; and p=0.045, Adjusted RR=0.47). All other Model 1 results, both unadjusted and adjusted, were nonsignificant (Table 12-11(a,b): p>0.19 for all remaining Model 1 contrasts).

Model 2 and Model 4 results were nonsignificant in both the unadjusted and adjusted analyses of SCL-90-R interpersonal sensitivity (Table 12-11(c,d,g,h): p≥0.35 for each analysis).

The unadjusted Model 3 analysis of SCL-90-R interpersonal sensitivity displayed two significant contrasts: the background dioxin category versus Comparisons and the low dioxin category versus Comparisons. In both contrasts, Comparisons had a higher SCL-90-R interpersonal sensitivity score than Ranch Hands (Table 12-11(e): p=0.034, Unadjusted RR=0.61; and p=0.010, Unadjusted RR=0.42, respectively). In the adjusted analysis, the contrast involving Ranch Hands in the background dioxin category became nonsignificant (Table 12-11(f): p=0.163), while the contrast involving Ranch Hands in the low dioxin category remained significant (Table 12-11(f): p=0.011, Adjusted RR=0.40). In addition, the adjusted Model 3 analysis of Ranch Hands in the low and high dioxin categories combined versus Comparisons was significant (Table 12-11(f): p=0.013, Adjusted RR=0.56). All other Model 3 unadjusted and adjusted results were nonsignificant (Table 12-11(e,f): p>0.05 for all remaining contrasts).

Table 12-11. Analysis of SCL-90-R Interpersonal Sensitivity

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*57 (7.4)*	*0.67 (0.48,0.93)*	*0.014**
	Comparison	*1,171*	*125 (10.7)*		
Officer	Ranch Hand	307	10 (3.3)	0.47 (0.23,0.97)	0.040*
	Comparison	461	31 (6.7)		
Enlisted Flyer	Ranch Hand	133	12 (9.0)	0.63 (0.31,1.31)	0.221
	Comparison	185	25 (13.5)		
Enlisted Groundcrew	Ranch Hand	332	35 (10.5)	0.78 (0.51,1.20)	0.257
	Comparison	525	69 (13.1)		

*: Statistically significant (0.01<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,884*	*0.65 (0.46,0.92)*	*0.013**
Officer	749	0.47 (0.23,0.98)	0.045*
Enlisted Flyer	305	0.66 (0.31,1.41)	0.287
Enlisted Groundcrew	830	0.74 (0.47,1.16)	0.195

*: Statistically significant (0.01<p-value≤0.050).

(c) MODEL 2: RANCH HANDS − INITIAL DIOXIN − UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	7 (5.0)	1.13 (0.87,1.46)	0.366
Medium	142	15 (10.6)		
High	138	11 (8.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 12-11. Analysis of SCL-90-R Interpersonal Sensitivity (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.05 (0.77,1.44)	0.745

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	125 (10.7)		
Background RH	351	24 (6.8)	0.61 (0.39,0.96)	0.034*
Low RH	210	10 (4.8)	0.42 (0.22,0.81)	0.010**
High RH	210	23 (11.0)	1.04 (0.65,1.66)	0.884
Low plus High RH	420	33 (7.9)	0.66 (0.43,1.01)	0.056

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

 *: Statistically significant (0.01<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	0.71 (0.44,1.15)	0.163
Low RH	201	0.40 (0.20,0.81)	0.011*
High RH	205	0.79 (0.48,1.31)	0.358
Low plus High RH	406	0.56 (0.36,0.88)	0.013*

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.01<p-value≤0.050).

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 12-11. Analysis of SCL-90-R Interpersonal Sensitivity (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	19 (7.3)	1.07 (0.90,1.26)	0.444
Medium	258	13 (5.0)		
High	254	25 (9.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
766	0.92 (0.77,1.10)	0.350

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.5 SCL-90-R Obsessive-compulsive Behavior

The obsessive-compulsive dimension reflects symptoms that are highly identified with the standard clinical syndrome of the same name. This measure focuses on thoughts, impulses, and actions that are experienced as unremitting and irresistible by the individual and inconsistent with the individual's own beliefs about what is desirable or reasonable. Behaviors and experiences of a more general cognitive performance attenuation also are included in this measure. The symptoms comprising the obsessive-compulsive dimension are experiencing repeated unpleasant thoughts that won't leave the mind, having trouble remembering things, worrying about sloppiness or carelessness, feeling blocked in getting things done, having to do things very slowly to ensure correctness, having to check and double-check what is done, having difficulty making decisions, having mind go blank, having trouble concentrating, and having to repeat the same actions (e.g., touching, counting, washing).

All unadjusted and adjusted results from the analysis of SCL-90-R obsessive-compulsive behavior were nonsignificant for Models 1, 2, and 3 (Table 12-12(a-f): p>0.08 for each test).

A significant positive association was revealed between the prevalence of high SCL-90-R obsessive-compulsive behavior scores and 1987 dioxin levels in the Model 4 unadjusted analysis (Table 12-12(g): p=0.043, Unadjusted RR=1.13), but after adjusting for covariates, the result became nonsignificant (Table 12-12(h): p=0.877).

Table 12-12. Analysis of SCL-90-R Obsessive-compulsive Behavior

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*125 (16.2)*	*0.87 (0.69,1.11)*	*0.274*
	Comparison	*1,171*	*212 (18.1)*		
Officer	Ranch Hand	307	31 (10.1)	0.83 (0.52,1.32)	0.431
	Comparison	461	55 (11.9)		
Enlisted Flyer	Ranch Hand	133	24 (18.0)	0.85 (0.48,1.50)	0.580
	Comparison	185	38 (20.5)		
Enlisted Groundcrew	Ranch Hand	332	70 (21.1)	0.91 (0.65,1.27)	0.586
	Comparison	525	119 (22.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,884*	*0.88 (0.68,1.13)*	*0.310*
Officer	749	0.85 (0.53,1.36)	0.492
Enlisted Flyer	305	0.89 (0.49,1.62)	0.713
Enlisted Groundcrew	830	0.89 (0.62,1.26)	0.505

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	15 (10.7)	1.15 (0.96,1.38)	0.140
Medium	142	29 (20.4)		
High	138	30 (21.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.06 (0.85,1.34)	0.589

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	212 (18.1)		
Background RH	351	50 (14.2)	0.78 (0.56,1.09)	0.151
Low RH	210	28 (13.3)	0.69 (0.45,1.05)	0.084
High RH	210	46 (21.9)	1.23 (0.85,1.76)	0.270
Low plus High RH	420	74 (17.6)	0.92 (0.68,1.24)	0.571

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	0.92 (0.64,1.31)	0.634
Low RH	201	0.69 (0.44,1.08)	0.105
High RH	205	0.97 (0.66,1.44)	0.888
Low plus High RH	406	0.82 (0.60,1.13)	0.219

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	33 (12.7)	1.13 (1.00,1.27)	0.043*
Medium	258	35 (13.6)		
High	254	56 (22.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.01<p-value$\leq$0.050).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
766	0.99 (0.86,1.13)	0.877

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.6 SCL-90-R Paranoid Ideation

The present dimension represents paranoid behavior fundamentally as a disordered mode of thinking. The cardinal characteristics of projective thought, hostility, suspiciousness, grandiosity, centrality, fear of loss of autonomy, and delusions are viewed as primary reflections of this disorder; item selection was oriented toward representing this conceptualization. The symptoms comprising the paranoid ideation dimension are feeling others are to blame for most of your troubles, feeling that most people cannot be trusted, feeling that you are watched or talked about by others, having ideas and beliefs that others do not share, not receiving proper credit from others for your achievements, and feeling that people will take advantage of you if you let them.

Significant differences between Ranch Hands and Comparisons were revealed in the Model 1 unadjusted analyses of SCL-90-R paranoid ideation across all occupations and within the enlisted groundcrew stratum (Table 12-13(a): p=0.010, Unadjusted RR=0.55; and p=0.032, Unadjusted RR=0.53, respectively). More Comparisons than Ranch Hands exhibited a high paranoid ideation score in both contrasts (Table 12-13(a): overall: 5.6% for Comparisons versus 3.1% for Ranch Hands; and enlisted groundcrew: 8.8% for Comparisons versus 4.8% for Ranch Hands). The same contrasts were significant in the adjusted analysis (Table 12-13(b): overall: p=0.011, Adjusted RR=0.53; and enlisted groundcrew: p=0.033, Adjusted RR=0.51). All other Model 1 contrasts were nonsignificant, as were all results from the Model 2 unadjusted and adjusted analysis (Table 12-13(a-d): p>0.15 for each nonsignificant result).

The Model 3 unadjusted analysis of SCL-90-R paranoid ideation revealed a significant contrast between Comparisons and Ranch Hands in the low dioxin category. More Comparisons (5.6%) than Ranch Hands in the low dioxin category (1.9%) had a high SCL-90-R paranoid ideation score (Table 12-13(e): p=0.032, Unadjusted RR=0.33). In the adjusted analysis of Model 3, this contrast was nonsignificant (Table 12-13(f): p=0.052). Another significant contrast was found in the unadjusted analysis between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 12-13(e): p=0.047, Unadjusted RR=0.52). More Comparisons (5.6%) than Ranch Hands (3.3%) had a high SCL-90-R paranoid ideation score. The contrast remained significant in the adjusted analysis (Table 12-13(f): p=0.019, Adjusted RR=0.45). All other Model 3 unadjusted and adjusted results were nonsignificant (Table 12-13(e,f): p>0.05 for each remaining contrast).

Results from both the unadjusted and adjusted analyses of SCL-90-R paranoid ideation in Model 4 were nonsignificant (Table 12-13(g,h): p>0.59 for each analysis).

Table 12-13. Analysis of SCL-90-R Paranoid Ideation

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*24 (3.1)*	*0.55 (0.34,0.88)*	*0.010***
	Comparison	*1,171*	*65 (5.6)*		
Officer	Ranch Hand	307	3 (1.0)	0.40 (0.11,1.46)	0.166
	Comparison	461	11 (2.4)		
Enlisted Flyer	Ranch Hand	133	5 (3.8)	0.86 (0.28,2.70)	0.802
	Comparison	185	8 (4.3)		
Enlisted Groundcrew	Ranch Hand	332	16 (4.8)	0.53 (0.29,0.95)	0.032*
	Comparison	525	46 (8.8)		

  *: Statistically significant (0.01<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,884*	*0.53 (0.32,0.88)*	*0.011**
Officer	749	0.39 (0.11,1.42)	0.153
Enlisted Flyer	305	0.85 (0.26,2.80)	0.793
Enlisted Groundcrew	830	0.51 (0.27,0.95)	0.033*

*: Statistically significant (0.01<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	3 (2.1)	1.08 (0.74,1.59)	0.690
Medium	142	6 (4.2)		
High	138	5 (3.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 12-13. Analysis of SCL-90-R Paranoid Ideation (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
416	1.06 (0.67,1.67)	0.803

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	65 (5.6)		
Background RH	351	10 (2.8)	0.51 (0.26,1.01)	0.052
Low RH	210	4 (1.9)	0.33 (0.12,0.91)	0.032*
High RH	210	10 (4.8)	0.83 (0.42,1.66)	0.605
Low plus High RH	420	14 (3.3)	0.52 (0.28,0.99)	0.047*

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.01 <$ p-value ≤ 0.050).

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	0.61 (0.30,1.26)	0.182
Low RH	201	0.35 (0.12,1.01)	0.052
High RH	205	0.58 (0.27,1.21)	0.147
Low plus High RH	406	0.45 (0.23,0.88)	0.019*

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.01 <$ p-value ≤ 0.050).

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 12-13. Analysis of SCL-90-R Paranoid Ideation (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	7 (2.7)	1.07 (0.83,1.38)	0.592
Medium	258	7 (2.7)		
High	254	10 (3.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
766	0.94 (0.72,1.22)	0.649

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.7 SCL-90-R Phobic Anxiety

Phobic anxiety is defined as a persistent fear response to a specific person, place, object, or situation that is characterized as being irrational and disproportionate to the stimulus and which leads to avoidance or escape behavior. The items of the present dimension focus on the more pathognomonic and disruptive manifestations of phobic behavior. The symptoms comprising the phobic anxiety dimension are feeling afraid in open spaces or on the street; feeling afraid to go out of the house alone; feeling afraid to travel on buses, subways, or trains; having to avoid certain things, places, or activities because they are frightening; feeling uneasy in crowds, such as while shopping or at a movie; feeling nervous when left alone; and feeling afraid of fainting in public.

All unadjusted and adjusted results from the analysis of SCL-90-R phobic anxiety for Models 1, 2, and 3 were nonsignificant (Table 12-14(a-f): p>0.07 for each analysis). The Model 4 unadjusted result from the analysis of SCL-90-R phobic anxiety was nonsignificant (Table 12-14(g): p=0.891). After adjusting for covariates, however, a significant inverse association between 1987 dioxin levels and a high SCL-90-R phobic anxiety score was found (Table 12-14(h): p=0.014, Adjusted RR=0.80).

Table 12-14. Analysis of SCL-90-R Phobic Anxiety

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*55*	*(7.1)*	*0.82 (0.58,1.16)*	*0.257*
	Comparison	*1,171*	*100*	*(8.5)*		
Officer	Ranch Hand	307	5	(1.6)	0.43 (0.16,1.18)	0.103
	Comparison	461	17	(3.7)		
Enlisted Flyer	Ranch Hand	133	13	(9.8)	0.85 (0.41,1.76)	0.654
	Comparison	185	21	(11.4)		
Enlisted Groundcrew	Ranch Hand	332	37	(11.1)	0.94 (0.61,1.44)	0.767
	Comparison	525	62	(11.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,884*	*0.82 (0.57,1.17)*	*0.275*
Officer	749	0.42 (0.15,1.15)	0.090
Enlisted Flyer	305	0.87 (0.40,1.85)	0.709
Enlisted Groundcrew	830	0.94 (0.60,1.48)	0.795

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	6 (4.3)	1.10 (0.84,1.45)	0.491
Medium	142	14 (9.9)		
High	138	10 (7.2)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	0.93 (0.67,1.31)	0.688

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

Table 12-14. Analysis of SCL-90-R Phobic Anxiety (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	100 (8.5)		
Background RH	351	25 (7.1)	0.85 (0.54,1.34)	0.487
Low RH	210	12 (5.7)	0.64 (0.35,1.19)	0.160
High RH	210	18 (8.6)	0.97 (0.57,1.65)	0.920
Low plus High RH	420	30 (7.1)	0.79 (0.51,1.22)	0.286

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	1.14 (0.70,1.85)	0.610
Low RH	201	0.67 (0.35,1.30)	0.234
High RH	205	0.66 (0.38,1.15)	0.141
Low plus High RH	406	0.67 (0.42,1.05)	0.078

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	18 (6.9)	1.01 (0.85,1.20)	0.891
Medium	258	14 (5.4)		
High	254	23 (9.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 12-14. Analysis of SCL-90-R Phobic Anxiety (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log$_2$ (1987 Dioxin)		
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
766	0.80 (0.66,0.96)	0.014*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.01<p-value≤0.050).

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.8 *SCL-90-R Psychoticism*

The psychoticism scale was developed in a fashion to represent the construct as a continuous dimension of human experience. Items indicative of a withdrawn, isolated, schizoid lifestyle were included, as were Schneiderian first-rank symptoms of schizophrenia, such as hallucinations and thought broadcasting. The symptoms comprising the psychoticism dimension are having the idea that someone else can control your thoughts, hearing voices that other people do not hear, believing that other people are aware of your private thoughts, having thoughts that are not your own, feeling lonely even when you are with people, having thoughts about sex that bother you a lot, believing that you should be punished for your sins, thinking that something serious is wrong with your body, never feeling close to another person, and thinking that something is wrong with your mind.

The unadjusted and adjusted analysis of SCL-90-R psychoticism displayed no significant results for Models 1 and 2 (Table 12-15(a-d): p>0.25 for each analysis).

A significant difference in the prevalence of high SCL-90-R psychoticism scores was found between Ranch Hands in the low dioxin category (5.7%) and Comparisons (10.5%) for the Model 3 unadjusted analysis (Table 12-15(e): p=0.030, Unadjusted RR=0.51). The difference was nonsignificant after adjusting for covariates (Table 12-15(f): p=0.055). All other Model 3 unadjusted and adjusted results, as well as the Model 4 unadjusted and adjusted analysis results, were nonsignificant (Table 12-15(e-h): p>0.13 for each remaining analysis).

Table 12-15. Analysis of SCL-90-R Psychoticism

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*69*	*(8.9)*	*0.84 (0.61,1.14)*	*0.255*
	Comparison	*1,171*	*123*	*(10.5)*		
Officer	Ranch Hand	307	18	(5.9)	0.89 (0.49,1.64)	0.718
	Comparison	461	30	(6.5)		
Enlisted Flyer	Ranch Hand	133	12	(9.0)	0.77 (0.37,1.63)	0.503
	Comparison	185	21	(11.4)		
Enlisted Groundcrew	Ranch Hand	332	39	(11.7)	0.84 (0.55,1.27)	0.404
	Comparison	525	72	(13.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,884*	*0.87 (0.63,1.20)*	*0.397*
Officer	749	0.92 (0.50,1.69)	0.784
Enlisted Flyer	305	0.78 (0.36,1.69)	0.528
Enlisted Groundcrew	830	0.88 (0.57,1.36)	0.558

(c) MODEL 2: RANCH HANDS − INITIAL DIOXIN − UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	8 (5.7)	1.14 (0.91,1.44)	0.260
Medium	142	18 (12.7)		
High	138	15 (10.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS − INITIAL DIOXIN − ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.15 (0.87,1.53)	0.325

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

Table 12-15. Analysis of Psychoticism (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	123 (10.5)		
Background RH	351	27 (7.7)	0.74 (0.48,1.15)	0.183
Low RH	210	12 (5.7)	0.51 (0.28,0.94)	0.030*
High RH	210	29 (13.8)	1.31 (0.85,2.03)	0.224
Low plus High RH	420	41 (9.8)	0.82 (0.55,1.22)	0.320

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.01<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	0.88 (0.56,1.40)	0.599
Low RH	201	0.54 (0.29,1.01)	0.055
High RH	205	1.12 (0.70,1.79)	0.642
Low plus High RH	406	0.78 (0.52,1.18)	0.242

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	17 (6.6)	1.12 (0.97,1.31)	0.135
Medium	258	21 (8.1)		
High	254	30 (11.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 12-15. Analysis of Psychoticism (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
766	1.03 (0.87,1.23)	0.700

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.9 SCL-90-R Somatization

The somatization dimension reflects distress arising from perceptions of bodily dysfunction. Complaints focusing on cardiovascular, gastrointestinal, respiratory, and other systems with strong autonomic mediation are included. Headaches, pain, and discomfort of the gross musculature and additional somatic equivalents of anxiety are components of the definition. These symptoms and signs have all been demonstrated to have high prevalence in disorders demonstrated to have a functional etiology, although all may be reflections of true physical disease. The symptoms comprising the somatization dimension are headaches, faintness or dizziness, pains in heart or chest, pains in lower back, nausea or upset stomach, soreness of muscles, trouble getting breath, hot or cold spells, numbness or tingling in parts of body, lump in throat, weakness in parts of body, and heavy feelings in arms or legs.

All unadjusted and adjusted results from the analysis of SCL-90-R somatization were nonsignificant for Models 1, 2, and 3 (Table 12-16(a-f): p>0.05 for each analysis).

The Model 4 unadjusted analysis of SCL-90-R somatization displayed a significant positive association between SCL-90-R somatization and 1987 dioxin levels (Table 12-16(g): p=0.015, Unadjusted RR=1.17). The adjusted analysis result was nonsignificant (Table 12-16(h): p=0.862).

Table 12-16. Analysis of SCL-90-R Somatization

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*104 (13.5)*	*0.90 (0.70,1.18)*	*0.451*
	Comparison	*1,171*	*172 (14.7)*		
Officer	Ranch Hand	307	21 (6.8)	0.89 (0.51,1.57)	0.695
	Comparison	461	35 (7.6)		
Enlisted Flyer	Ranch Hand	133	26 (19.5)	1.08 (0.61,1.90)	0.792
	Comparison	185	34 (18.4)		
Enlisted Groundcrew	Ranch Hand	332	57 (17.2)	0.85 (0.59,1.21)	0.370
	Comparison	525	103 (19.6)		

Table 12-16. Analysis of SCL-90-R Somatization (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,884*	*0.90 (0.68,1.19)*	*0.452*
Officer	749	0.93 (0.52,1.64)	0.799
Enlisted Flyer	305	1.14 (0.63,2.05)	0.670
Enlisted Groundcrew	830	0.81 (0.56,1.18)	0.267

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	13 (9.3)	1.20 (0.99,1.46)	0.066
Medium	142	23 (16.2)		
High	138	27 (19.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.16 (0.91,1.47)	0.226

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

Table 12-16. Analysis of SCL-90-R Somatization (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	172 (14.7)		
Background RH	351	40 (11.4)	0.81 (0.56,1.17)	0.253
Low RH	210	21 (10.0)	0.63 (0.39,1.01)	0.057
High RH	210	42 (20.0)	1.36 (0.93,1.99)	0.111
Low plus High RH	420	63 (15.0)	0.92 (0.67,1.28)	0.630

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	0.97 (0.66,1.45)	0.898
Low RH	201	0.64 (0.38,1.06)	0.081
High RH	205	1.02 (0.68,1.52)	0.932
Low plus High RH	406	0.81 (0.57,1.14)	0.223

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	27 (10.4)	1.17 (1.03,1.33)	0.015*
Medium	258	27 (10.5)		
High	254	49 (19.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.01<p-value$\leq$0.050).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 12-16. Analysis of SCL-90-R Somatization (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
766	1.01 (0.88,1.17)	0.862

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.10   SCL-90-R GSI

The GSI represents the best single indicator of the current level or depth of the disorder and should be used in most instances in which a single summary measure is required. The GSI combines information on numbers of symptoms and intensity of perceived distress.

No significant results were found from the analysis of SCL-90-R GSI from Models 1, 2, or 3 in either the unadjusted or adjusted analyses (Table 12-17(a-f): p>0.07 for each analysis).

The Model 4 unadjusted analysis of SCL-90-R GSI displayed a positive significant association between 1987 dioxin levels and a prevalence of high GSI scores (Table 12-17(g): p=0.040, Unadjusted RR=1.16). The association became nonsignificant after adjusting for covariates (Table 12-17(h): p=0.672).

Table 12-17. Analysis of SCL-90-R GSI

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*81 (10.5)*	*0.84 (0.63,1.13)*	*0.243*
	Comparison	*1,171*	*143 (12.2)*		
Officer	Ranch Hand	307	14 (4.6)	0.69 (0.36,1.32)	0.258
	Comparison	461	30 (6.5)		
Enlisted Flyer	Ranch Hand	133	12 (9.0)	0.67 (0.32,1.38)	0.275
	Comparison	185	24 (13.0)		
Enlisted Groundcrew	Ranch Hand	332	55 (16.6)	0.97 (0.67,1.41)	0.883
	Comparison	525	89 (17.0)		

Table 12-17. Analysis of SCL-90-R GSI (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1,884***	***0.81 (0.59,1.10)***	***0.166***
Officer	749	0.69 (0.36,1.33)	0.268
Enlisted Flyer	305	0.67 (0.31,1.42)	0.297
Enlisted Groundcrew	830	0.90 (0.61,1.33)	0.592

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	13 (9.3)	1.10 (0.89,1.36)	0.398
Medium	142	20 (14.1)		
High	138	18 (13.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.01 (0.77,1.31)	0.966

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

Table 12-17. Analysis of SCL-90-R GSI (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	143 (12.2)		
Background RH	351	29 (8.3)	0.68 (0.45,1.04)	0.076
Low RH	210	18 (8.6)	0.66 (0.39,1.11)	0.115
High RH	210	33 (15.7)	1.28 (0.84,1.93)	0.246
Low plus High RH	420	51 (12.1)	0.92 (0.65,1.31)	0.639

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	0.81 (0.52,1.27)	0.353
Low RH	201	0.65 (0.37,1.13)	0.123
High RH	205	0.90 (0.58,1.40)	0.639
Low plus High RH	406	0.76 (0.52,1.11)	0.160

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	19 (7.3)	1.16 (1.01,1.34)	0.040*
Medium	258	24 (9.3)		
High	254	37 (14.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant ($0.01 < \text{p-value} \leq 0.050$).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 12-17. Analysis of SCL-90-R GSI (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (1987 Dioxin) | |
| | **Adjusted Relative Risk** | |
n	**(95% C.I.)^a**	**p-Value**
766	0.97 (0.83,1.13)	0.672

^{a}Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.11   SCL-90-R PST

The PST is simply a count of the number of symptoms the participant reports as experiencing to any degree. When used configurally in conjunction with the GSI, information on style of response and numbers of symptoms endorsed can be helpful in appreciating the clinical picture.

Both the unadjusted and adjusted Model 1 analyses of SCL-90-R PST revealed a significant inverse association between Ranch Hands and Comparisons when examined across all occupational strata (Table 12-18(a,b): p=0.042, Unadjusted RR=0.74; and p=0.033, Adjusted RR=0.72, respectively). More Comparisons (12.6%) than Ranch Hands (9.6%) exhibited a high PST score. All other Model 1 unadjusted and adjusted contrasts, as well as each of the unadjusted and adjusted Model 2 analyses, were nonsignificant (Table 12-18(a-d): p>0.11 for analysis).

The Model 3 unadjusted analysis of SCL-90-R PST displayed a significant difference between Ranch Hands in the low dioxin category (8.5%) and Comparisons (12.6%) with a high PST score (Table 12-18(e): p=0.014, Unadjusted RR=0.49). The result remained significant in the adjusted analysis (Table 12-18(f): p=0.019, Adjusted RR=0.49). The adjusted analysis also found a significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 12-18(f): p=0.025, Adjusted RR=0.64). Similarly, more Comparisons than Ranch Hands displayed a high PST score in this contrast. All other Model 3 unadjusted and adjusted contrasts and each result from the Model 4 unadjusted and adjusted analysis were nonsignificant (Table 12-18(e-h): p>0.07 for each remaining analysis).

Table 12-18. Analysis of SCL-90-R PST

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*74 (9.6)*	*0.74 (0.55,0.99)*	*0.042**
	Comparison	*1,171*	*147 (12.6)*		
Officer	Ranch Hand	307	16 (5.2)	0.63 (0.34,1.15)	0.135
	Comparison	461	37 (8.0)		
Enlisted Flyer	Ranch Hand	133	11 (8.3)	0.67 (0.31,1.43)	0.299
	Comparison	185	22 (11.9)		
Enlisted Groundcrew	Ranch Hand	332	47 (14.2)	0.82 (0.56,1.20)	0.308
	Comparison	525	88 (16.8)		

*: Statistically significant (0.01<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,884*	*0.72 (0.53,0.98)*	*0.033**
Officer	749	0.61 (0.33,1.13)	0.117
Enlisted Flyer	305	0.69 (0.31,1.50)	0.345
Enlisted Groundcrew	830	0.78 (0.52,1.17)	0.227

*: Statistically significant (0.01<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	10 (7.1)	1.02 (0.81,1.29)	0.865
Medium	142	20 (14.1)		
High	138	14 (10.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 12-18. Analysis of SCL-90-R PST (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
416	0.96 (0.72,1.28)	0.778

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	147 (12.6)		
Background RH	351	30 (8.5)	0.68 (0.45,1.03)	0.071
Low RH	210	14 (6.7)	0.49 (0.28,0.86)	0.014*
High RH	210	30 (14.3)	1.11 (0.73,1.70)	0.624
Low plus High RH	420	44 (10.5)	0.74 (0.51,1.08)	0.113

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.01<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	0.80 (0.52,1.23)	0.299
Low RH	201	0.49 (0.27,0.89)	0.019*
High RH	205	0.83 (0.52,1.31)	0.413
Low plus High RH	406	0.64 (0.43,0.94)	0.025*

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.01<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 12-18. Analysis of SCL-90-R PST (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	20 (7.7)	1.08 (0.93,1.25)	0.324
Medium	258	21 (8.1)		
High	254	33 (13.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
766	0.92 (0.79,1.09)	0.341

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.12 SCL-90-R PSDI

The PSDI is a pure intensity measure, in a sense, "corrected" for numbers of symptoms. It functions primarily as a measure of response style in the sense of communicating whether the patient is "augmenting" or "attenuating" symptomatic distress in his style of reporting his disorder.

More Comparisons (15.1%) than Ranch Hands (7.5%) had a high SCL-90-R PSDI score within the enlisted flyer stratum in the Model 1 unadjusted and adjusted analysis (Table 12-19 (a,b): p=0.043, Unadjusted RR=0.46; and p=0.036, Adjusted RR=0.43, respectively). All other Model 1 unadjusted and adjusted contrasts were nonsignificant (Table 12-19(a,b): p≥0.34 for each contrast). Results from each Model 2 and 3 unadjusted and adjusted analysis were also nonsignificant (Table 12-19(c-f): p>0.09 for each analysis).

A significant positive relation between 1987 dioxin levels and prevalence of high PSDI scores was found from the unadjusted Model 4 analysis (Table 12-19(g): p=0.016, Adjusted RR=1.23). The relation became nonsignificant after adjusting for covariates (Table 12-19(h): p=0.497).

Table 12-19. Analysis of SCL-90-R PSDI

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*772*	*55 (7.1)*	*0.86 (0.61,1.21)*	*0.385*
	Comparison	*1,171*	*96 (8.2)*		
Officer	Ranch Hand	307	10 (3.3)	1.16 (0.50,2.68)	0.728
	Comparison	461	13 (2.8)		
Enlisted Flyer	Ranch Hand	133	10 (7.5)	0.46 (0.21,0.97)	0.043*
	Comparison	185	28 (15.1)		
Enlisted Groundcrew	Ranch Hand	332	35 (10.5)	1.01 (0.64,1.58)	0.976
	Comparison	525	55 (10.5)		

*: Statistically significant (0.01<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,884*	*0.84 (0.59,1.20)*	*0.340*
Officer	749	0.99 (0.41,2.35)	0.976
Enlisted Flyer	305	0.43 (0.20,0.95)	0.036*
Enlisted Groundcrew	830	1.04 (0.65,1.64)	0.877

*: Statistically significant (0.01<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	10 (7.1)	1.09 (0.85,1.40)	0.489
Medium	142	16 (11.3)		
High	138	10 (7.2)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 12-19. Analysis of SCL-90-R PSDI (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
416	1.05 (0.78,1.42)	0.727

[a]Relative risk for a twofold increase in initial dioxin.

Note: Current total household income was not included in the model (see Section 12.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	96 (8.2)		
Background RH	351	18 (5.1)	0.64 (0.38,1.08)	0.096
Low RH	210	15 (7.1)	0.84 (0.48,1.49)	0.556
High RH	210	21 (10.0)	1.18 (0.72,1.95)	0.517
Low plus High RH	420	36 (8.6)	1.00 (0.66,1.50)	0.991

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	0.81 (0.47,1.40)	0.450
Low RH	201	0.83 (0.45,1.52)	0.546
High RH	205	0.84 (0.50,1.41)	0.503
Low plus High RH	406	0.83 (0.54,1.28)	0.402

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 12-19. Analysis of SCL-90-R PSDI (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	8 (3.1)	1.23 (1.04,1.46)	0.016*
Medium	258	20 (7.8)		
High	254	26 (10.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.01<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
748	1.07 (0.89,1.28)	0.497

[a]Relative risk for a twofold increase in 1987 dioxin.

12.2.2.2.13   *WMS-R Verbal Paired Associates*

All results from the analysis of WMS-R Verbal Paired Associates test for Model 1 through Model 3 were nonsignificant, both unadjusted and adjusted for covariates (Table 12-20(a-f): p>0.15 for each analysis).

The unadjusted Model 4 analysis of WMS-R Verbal Paired Associates test revealed an inverse significant association between 1987 dioxin levels and WMS-R Verbal Paired Associates scores (Table 12-20(g): p=0.020, Slope=-0.168). As 1987 dioxin increased, the scores on the Verbal Paired Associates test decreased. In the adjusted analysis, the relation became nonsignificant after adjusting for covariates (Table 12-20(h): p=0.458).

Table 12-20. Analysis of WMS-R Verbal Paired Associates

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*11.02*	*0.06 (-0.23,0.35)*	*0.674*
	Comparison	*1,169*	*10.96*		
Officer	Ranch Hand	307	11.65	0.12 (-0.34,0.57)	0.615
	Comparison	461	11.54		
Enlisted Flyer	Ranch Hand	133	10.00	-0.23 (-0.94,0.47)	0.520
	Comparison	184	10.23		
Enlisted Groundcrew	Ranch Hand	333	10.85	0.14 (-0.29,0.58)	0.526
	Comparison	524	10.71		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*10.78*	*0.07 (-0.21,0.35)*	*0.622*
	Comparison	*1,164*	*10.71*		
Officer	Ranch Hand	307	11.72	0.18 (-0.26,0.63)	0.421
	Comparison	460	11.53		
Enlisted Flyer	Ranch Hand	131	10.18	-0.20 (-0.89,0.50)	0.581
	Comparison	182	10.38		
Enlisted Groundcrew	Ranch Hand	330	10.37	0.07 (-0.36,0.49)	0.753
	Comparison	522	10.30		

Note: Current total household income was not included in the model (see Section 12.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	140	11.05	11.04	0.001	-0.074 (0.122)	0.546
Medium	143	10.67	10.67			
High	138	10.75	10.76			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 12-20. Analysis of WMS-R Verbal Paired Associates (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	140	10.83	0.085	-0.042 (0.142)	0.767
Medium	142	10.51			
High	135	10.67			

Note: Current total household income was not included in the model (see Section 12.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,169	10.96	10.96		
Background RH	351	11.26	11.24	0.28 (-0.10,0.67)	0.154
Low RH	211	10.82	10.82	-0.14 (-0.61,0.33)	0.567
High RH	210	10.83	10.86	-0.10 (-0.58,0.37)	0.664
Low plus High RH	421	10.82	10.84	-0.12 (-0.48,0.24)	0.507

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,164	10.72		
Background RH	350	10.79	0.08 (-0.30,0.46)	0.690
Low RH	210	10.73	0.01 (-0.44,0.47)	0.953
High RH	207	10.83	0.12 (-0.36,0.59)	0.625
Low plus High RH	417	10.78	0.07 (-0.29,0.42)	0.715

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

    Current total household income was not included in the model (see Section 12.1.4).

Table 12-20.   Analysis of WMS-R Verbal Paired Associates (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean**	**R^2**	**Slope (Standard Error)**	**p-Value**
Low	259	11.36	0.007	-0.168 (0.072)	0.020*
Medium	258	10.98			
High	255	10.72			

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

*: Statistically significant (0.01<p-value≤0.050).

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	259	10.71	0.073	-0.060 (0.081)	0.458
Medium	257	10.64			
High	251	10.62			

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.14   WMS-R Logical Memory, Immediate Recall

No significant results were found within the unadjusted or adjusted analyses of the immediate recall for the WMS-R Logical Memory test for Models 1, 2, or 3 (Table 12-21(a-f): p≥0.06 for each analysis). A significant inverse relation between 1987 dioxin levels and the immediate recall scores for the Logical Memory test was found from the Model 4 unadjusted analysis (Table 12-21(g): p=0.001, Slope=-0.237). As 1987 dioxin increased, the scores on this test decreased. After adjusting for covariates, however, the result became nonsignificant (Table 12-21(h): p=0.541).

Table 12-21. Analysis of WMS-R Logical Memory, Immediate Recall

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*11.70*	*0.12 (-0.18,0.42)*	*0.431*
	Comparison	*1,169*	*11.58*		
Officer	Ranch Hand	307	12.59	-0.01 (-0.48,0.45)	0.957
	Comparison	461	12.60		
Enlisted Flyer	Ranch Hand	133	10.66	-0.26 (-0.97,0.46)	0.483
	Comparison	184	10.92		
Enlisted Groundcrew	Ranch Hand	333	11.30	0.38 (-0.06,0.83)	0.089
	Comparison	524	10.91		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*11.46*	*0.12 (-0.16,0.41)*	*0.397*
	Comparison	*1,164*	*11.34*		
Officer	Ranch Hand	307	12.50	0.06 (-0.39,0.51)	0.786
	Comparison	460	12.44		
Enlisted Flyer	Ranch Hand	131	10.89	-0.24 (-0.94,0.46)	0.505
	Comparison	182	11.13		
Enlisted Groundcrew	Ranch Hand	330	10.88	0.31 (-0.12,0.75)	0.153
	Comparison	522	10.57		

Note: Current total household income was not included in the model (see Section 12.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	140	12.02	12.03	0.007	-0.207 (0.123)	0.095
Medium	143	11.16	11.16			
High	138	11.28	11.27			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	134	11.33	0.127	-0.007 (0.142)	0.961
Medium	138	10.77			
High	134	11.11			

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,169	11.58	11.58		
Background RH	351	11.97	11.96	0.38 (-0.02,0.78)	0.060
Low RH	211	11.78	11.78	0.20 (-0.29,0.68)	0.422
High RH	210	11.19	11.20	-0.38 (-0.87,0.11)	0.126
Low plus High RH	421	11.49	11.49	-0.09 (-0.46,0.28)	0.632

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,164	11.33		
Background RH	350	11.39	0.06 (-0.33,0.44)	0.776
Low RH	210	11.67	0.33 (-0.13,0.79)	0.158
High RH	207	11.38	0.05 (-0.43,0.53)	0.844
Low plus High RH	417	11.52	0.19 (-0.16,0.55)	0.291

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

     Current total household income was not included in the model (see Section 12.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean	R^2	Slope (Standard Error)	p-Value
Low	259	12.15	0.013	-0.237 (0.073)	0.001**
Medium	258	11.88			
High	255	11.08			

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

**: Statistically significant (p-value≤0.010).

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	259	11.31	0.093	-0.050 (0.082)	0.541
Medium	257	11.39			
High	251	10.96			

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.15 WMS-R Logical Memory, Delayed Recall

The Model 1 unadjusted and adjusted analyses of the delayed recall portion of the WMS-R Logical Memory test revealed a significant difference in means between Ranch Hands and Comparisons within the enlisted groundcrew stratum (Table 12-22(a,b): p=0.021, difference of means=0.57; and p=0.039, difference of means =0.50, respectively). Mean scores were higher for Ranch Hands than for Comparisons. All other Model 1 unadjusted and adjusted contrasts and each Model 2 unadjusted and adjusted analysis were nonsignificant (Table 12-22(a-d): p>0.18 for each contrast).

A significant difference in means was found from the unadjusted analysis of the delayed recall portion of the WMS-R Logical Memory test from Model 3, contrasting Ranch Hands in the background dioxin category with Comparisons (Table 12-22(e): p=0.027, difference of means=0.49). The difference was nonsignificant after adjusting for covariates (Table 12-22(f): p=0.612). All other Model 3 unadjusted and adjusted results were nonsignificant (Table 12-22(e,f): p>0.12 for each result).

The Model 4 unadjusted analysis of the delayed recall portion of the WMS-R Logical Memory test revealed an inverse significant relation between 1987 dioxin levels and logical memory, delayed recall scores (Table 12-22(g): p=0.004, Slope=-0.237). As 1987 dioxin increased, the scores on this test decreased. The relation was nonsignificant after adjusting for covariates (Table 12-22(h): p=0.762).

Table 12-22. Analysis of WMS-R Logical Memory, Delayed Recall

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*9.59*	*0.19 (-0.14,0.53)*	*0.250*
	Comparison	*1,168*	*9.40*		
Officer	Ranch Hand	307	10.58	-0.08 (-0.59,0.43)	0.770
	Comparison	460	10.65		
Enlisted Flyer	Ranch Hand	133	8.41	-0.16 (-0.94,0.63)	0.696
	Comparison	184	8.57		
Enlisted Groundcrew	Ranch Hand	333	9.16	0.57 (0.08,1.05)	0.021*
	Comparison	524	8.59		

*: Statistically significant (0.01<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*9.05*	*0.20 (-0.11,0.52)*	*0.197*
	Comparison	*1,163*	*8.84*		
Officer	Ranch Hand	307	10.15	0.01 (-0.48,0.51)	0.954
	Comparison	459	10.13		
Enlisted Flyer	Ranch Hand	131	8.44	-0.11 (-0.87,0.66)	0.782
	Comparison	182	8.55		
Enlisted Groundcrew	Ranch Hand	330	8.46	0.50 (0.02,0.97)	0.039*
	Comparison	522	7.97		

*: Statistically significant (0.01<p-value≤0.050).

Note: Current total household income was not included in the model (see Section 12.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	140	9.80	9.81	0.005	-0.185 (0.140)	0.188
Medium	143	9.09	9.09			
High	138	9.16	9.15			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 12-22. Analysis of WMS-R Logical Memory, Delayed Recall (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	140	8.87	0.134	-0.007 (0.159)	0.965
Medium	142	8.36			
High	135	8.76			

Note: Current total household income was not included in the model (see Section 12.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,168	9.40	9.40		
Background RH	351	9.90	9.89	0.49 (0.06,0.93)	0.027*
Low RH	211	9.58	9.58	0.18 (-0.35,0.71)	0.509
High RH	210	9.12	9.13	-0.27 (-0.81,0.27)	0.328
Low plus High RH	421	9.35	9.36	-0.04 (-0.45,0.36)	0.835

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

*: Statistically significant (0.01<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,163	8.85		
Background RH	350	8.96	0.11 (-0.31,0.53)	0.612
Low RH	210	9.18	0.33 (-0.17,0.84)	0.195
High RH	207	9.12	0.27 (-0.25,0.79)	0.311
Low plus High RH	417	9.15	0.30 (-0.09,0.69)	0.127

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

    Current total household income was not included in the model (see Section 12.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean**	**R^2**	**Slope (Standard Error)**	**p-Value**
Low	259	10.08	0.011	-0.237 (0.082)	0.004**
Medium	258	9.73			
High	255	8.97			

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

**: Statistically significant (p-value≤0.010).

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	259	8.73	0.103	-0.028 (0.091)	0.762
Medium	257	8.81			
High	251	8.45			

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Current total household income was not included in the model (see Section 12.1.4).

12.2.2.2.16 WMS-R Visual Reproduction, Immediate Recall

No results from either the unadjusted and adjusted analyses of the immediate recall portion of the WMS-R Visual Reproduction test were significant in Model 1 through Model 4 (Table 12-23(a-h): p≥0.09 for each analysis).

Table 12-23. Analysis of WMS-R Visual Reproduction, Immediate Recall

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*27.94*	*0.10 (-0.34,0.54)*	*0.663*
	Comparison	*1,167*	*27.84*		
Officer	Ranch Hand	307	28.79	0.01 (-0.68,0.70)	0.973
	Comparison	461	28.78		
Enlisted Flyer	Ranch Hand	133	25.99	-0.46 (-1.52,0.60)	0.395
	Comparison	183	26.45		
Enlisted Groundcrew	Ranch Hand	333	27.93	0.43 (-0.22,1.08)	0.197
	Comparison	523	27.50		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*749*	*27.32*	*0.15 (-0.26,0.55)*	*0.480*
	Comparison	*1,132*	*27.17*		
Officer	Ranch Hand	299	28.69	0.13 (-0.50,0.77)	0.680
	Comparison	450	28.56		
Enlisted Flyer	Ranch Hand	129	26.22	-0.49 (-1.48,0.51)	0.337
	Comparison	174	26.71		
Enlisted Groundcrew	Ranch Hand	321	26.87	0.39 (-0.22,1.01)	0.207
	Comparison	508	26.47		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	140	27.98	27.97	0.001	-0.053 (0.187)	0.777
Medium	143	27.34	27.33			
High	138	27.68	27.69			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	140	28.15	0.190	-0.025 (0.203)	0.902
Medium	142	27.51			
High	135	27.87			

Note: Current total household income was not included in the model (see Section 12.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,167	27.84	27.85		
Background RH	351	28.31	28.20	0.36 (-0.22,0.94)	0.226
Low RH	211	27.62	27.65	-0.19 (-0.90,0.51)	0.589
High RH	210	27.71	27.81	-0.03 (-0.74,0.68)	0.925
Low plus High RH	421	27.66	27.73	-0.11 (-0.65,0.42)	0.676

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,132	27.20		
Background RH	342	27.31	0.12 (-0.42,0.66)	0.676
Low RH	201	27.43	0.23 (-0.43,0.89)	0.487
High RH	205	27.33	0.14 (-0.54,0.81)	0.688
Low plus High RH	406	27.38	0.19 (-0.32,0.69)	0.470

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean	R^2	Slope (Standard Error)	p-Value
Low	259	28.34	0.004	-0.183 (0.108)	0.090
Medium	258	28.03			
High	255	27.49			

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	252	27.23	0.157	-0.054 (0.116)	0.643
Medium	249	27.42			
High	247	26.83			

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

12.2.2.2.17   WMS-R Visual Reproduction, Delayed Recall

All results from both the unadjusted and adjusted analyses of the delayed recall portion of the WMS-R Visual Reproduction test were nonsignificant for Model 1 through Model 4 (Table 12-24(a-h): p>0.05 for each analysis).

Table 12-24. Analysis of WMS-R Visual Reproduction, Delayed Recall

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*773*	*26.34*	*0.24 (-0.34,0.83)*	*0.409*
	Comparison	*1,167*	*26.09*		
Officer	Ranch Hand	307	27.47	0.10 (-0.81,1.01)	0.834
	Comparison	461	27.38		
Enlisted Flyer	Ranch Hand	133	24.05	-0.42 (-1.82,0.99)	0.560
	Comparison	183	24.47		
Enlisted Groundcrew	Ranch Hand	333	26.20	0.67 (-0.19,1.54)	0.127
	Comparison	523	25.53		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*749*	*25.34*	*0.33 (-0.20,0.86)*	*0.221*
	Comparison	*1,132*	*25.01*		
Officer	Ranch Hand	299	27.03	0.29 (-0.55,1.13)	0.497
	Comparison	450	26.74		
Enlisted Flyer	Ranch Hand	129	24.29	-0.34 (-1.65,0.97)	0.615
	Comparison	174	24.63		
Enlisted Groundcrew	Ranch Hand	321	24.51	0.62 (-0.19,1.42)	0.132
	Comparison	508	23.89		

Table 12-24. Analysis of WMS-R Visual Reproduction, Delayed Recall (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	140	25.95	25.93	0.002	0.035 (0.237)	0.884
Medium	143	25.98	25.97			
High	138	25.95	25.98			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	134	26.01	0.221	0.077 (0.254)	0.762
Medium	138	26.24			
High	134	26.18			

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,167	26.09	26.10		
Background RH	351	26.83	26.72	0.62 (-0.14,1.39)	0.112
Low RH	211	25.98	26.01	-0.08 (-1.02,0.85)	0.861
High RH	210	25.94	26.05	-0.05 (-0.99,0.89)	0.922
Low plus High RH	421	25.96	26.03	-0.07 (-0.78,0.65)	0.858

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 12-24. Analysis of WMS-R Visual Reproduction, Delayed Recall (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,132	25.03		
Background RH	342	25.32	0.30 (-0.41,1.01)	0.413
Low RH	201	25.53	0.50 (-0.36,1.37)	0.256
High RH	205	25.28	0.26 (-0.63,1.14)	0.573
Low plus High RH	406	25.40	0.38 (-0.28,1.04)	0.263

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean	R^2	Slope (Standard Error)	p-Value
Low	259	27.15	0.005	-0.272 (0.139)	0.051
Medium	258	25.92			
High	255	25.98			

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	252	25.38	0.175	-0.090 (0.148)	0.541
Medium	249	24.87			
High	247	25.01			

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

12.3   DISCUSSION

The AFHS assessed cognitive and psychopathological functioning using the Verbal Paired Associates, Logical Memory, and the Visual Reproduction tests from the WMS-R and 12 SCL-90-R subscales. Both the WMS-R and the SCL-90-R have been found valid and reliable for these purposes. In prior years of the AFHS, cognitive functioning had been assessed using other tests, such as the HRB, the WAIS-Revised, and the WMS. Psychopathology had been studied in previous follow-up examinations with other measures, such as the MMPI, the CMI, and the MCMI. For the 2002 AFHS, the WMS-R was chosen in large part due to prior findings that used the WMS and found small decreases in memory skills

among the Ranch Hand veterans (40). The SCL-90-R was selected in part because of ease and brevity of administration.

Memory, in basic terms, involves the perception and encoding of information, followed by the retrieval of this stored information. One way of measuring memory functioning is to present material to a participant and then record the accuracy with which he is able to repeat the information. The time between the initial presentation and the recall can vary. A time gap of less than a minute is considered immediate recall, while a 30-minute time gap is considered delayed recall. Both immediate and delayed recall are considered short-term memory. This is in contrast to long-term memory, in which the time gap would be in terms of days, weeks, months or years. When memory impairment occurs, it is typically more evident in short-term memory rather than long-term memory. Memory can be adversely impacted by a variety of influences, such as emotional state, physical injury, or chemical exposure. One of the purposes of the AFHS was to evaluate whether exposure to herbicides led to decreased short-term memory skills.

Psychopathology is a more complex concept than memory because it often involves the interplay of such things as deep-rooted personality traits, coping skills, chronic and situational stressors, and biochemical changes. A person's reported symptoms are clustered into categories that are labeled as psychopathological states (e.g., depression, anxiety, and paranoia). The 2002 AFHS evaluated the possible influence of exposure to herbicides based on the presence of these psychopathological states in the study participants.

The results from investigating the associations of the memory assessment with covariates were generally in line with expectations. Memory skills decrease as a person ages. Scores on memory tests are higher for college-educated, wealthier, employed officers than for high-school educated, less wealthy, not employed, enlisted men. Memory has a moderate correlation to intelligence (55) and intelligence is correlated with success in education and employment.

The SCL-90-R results showed a similar trend to the results from the WMS-R, with lower income, less educated, not employed, enlisted men reporting more overall psychopathology, evidenced by higher scores on the anxiety, depression, hostility, interpersonal sensitivity, obsessive-compulsive, paranoid ideation, phobic anxiety, psychoticism, and somatization scales.

Test results indicate there were no adverse effects for the Ranch Hand group as compared to the Comparisons. In fact, the Ranch Hand group displayed fewer symptoms of psychological distress with a smaller prevalence of abnormally high scores on the interpersonal sensitivity, paranoid ideation, and phobic anxiety scales. None of the memory functioning and psychopathology scales were adversely associated with exposure to herbicides or dioxin.

12.4 SUMMARY

The psychology assessment was based on questionnaire data, which was subsequently verified by a review of medical records, and data from the SCL-90-R and the WMS-R. Associations with herbicide exposure (i.e., group – Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable in the psychology assessment. The significant adjusted results are discussed in the sections below.

12.4.1 Model 1: Group Analysis

Model 1 analyses examined differences between Ranch Hands and Comparisons across all occupations and within each occupational stratum. Each significant result in the adjusted analysis revealed more Comparisons than Ranch Hands with either a history of other neuroses or with a high score on an SCL-90-R scale. More Comparisons than Ranch Hands had high scores on the SCL-90-R interpersonal sensitivity, paranoid ideation, and PST scales. More Comparison officers than Ranch Hand officers had a history of other neuroses and had high scores on the SCL-90-R interpersonal sensitivity scale. More Comparison enlisted flyers than Ranch Hand enlisted flyers had high scores on the SCL-90-R PSDI. More Comparison enlisted groundcrew than Ranch Hand enlisted groundcrew had high scores on the SCL-90-R paranoid ideation scale. Comparison enlisted groundcrew had a lower mean score on the delayed recall of the Logical Memory test of the WMS-R than Ranch Hand enlisted groundcrew. Table 12-25 displays the results of the group analysis.

Table 12-25. Summary of Group Analysis (Model 1) for Psychology Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Psychoses (D)	ns	ns	NS	ns
Alcohol Dependence (D)	NS	ns	ns	NS
Drug Dependence (D)	ns	ns	--	ns
Anxiety (D)	NS	ns	NS	NS
Other Neuroses (D)	ns	p=0.029 (0.72)	NS	NS
Psychological Examination				
SCL-90-R Anxiety (D)	ns	ns	ns	NS
SCL-90-R Depression (D)	ns	ns	ns	NS
SCL-90-R Hostility (D)	ns	ns	ns	NS
SCL-90-R Interpersonal Sensitivity (D)	p=0.014 (0.67)	p=0.040 (0.47)	ns	ns
SCL-90-R Obsessive-compulsive Behavior (D)	ns	ns	ns	ns
SCL-90-R Paranoid Ideation (D)	p=0.010 (0.55)	ns	ns	p=0.032 (0.53)
SCL-90-R Phobic Anxiety (D)	ns	ns	ns	ns
SCL-90-R Psychoticism (D)	ns	ns	ns	ns
SCL-90-R Somatization (D)	ns	ns	NS	ns
SCL-90-R GSI (D)	ns	ns	ns	ns
SCL-90-R PST (D)	p=0.042 (0.74)	ns	ns	ns
SCL-90-R PSDI (D)	ns	NS	p=0.043 (0.46)	NS
WMS-R Verbal Paired Associates (C)[a]	NS	NS	ns	NS
WMS-R Logical Memory, Immediate Recall (C)[a]	NS	ns	ns	NS
WMS-R Logical Memory, Delayed Recall (C)[a]	NS	ns	ns	p=0.021 (0.57)
WMS-R Visual Reproduction, Immediate Recall (C)[a]	NS	NS	ns	NS
WMS-R Visual Reproduction, Delayed Recall (C)[a]	NS	NS	ns	NS

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
C: Continuous form of dependent variable.
D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

	ADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Medical Records				
Psychoses (D)	ns	ns	NS	ns
Alcohol Dependence (D)	NS	ns	ns	NS
Drug Dependence (D)	ns	--	--	ns
Anxiety (D)	NS	ns	NS	NS
Other Neuroses (D)	NS	p=0.043 (0.73)	NS	NS
Psychology Examination				
SCL-90-R Anxiety (D)	ns	ns	ns	NS
SCL-90-R Depression (D)	ns	ns	ns	ns
SCL-90-R Hostility (D)	ns	ns	ns	NS
SCL-90-R Interpersonal Sensitivity (D)	p=0.013 (0.65)	p=0.045 (0.47)	ns	ns
SCL-90-R Obsessive-compulsive Behavior (D)	ns	ns	ns	ns
SCL-90-R Paranoid Ideation (D)	p=0.011 (0.53)	ns	ns	p=0.033 (0.51)
SCL-90-R Phobic Anxiety (D)	ns	ns	ns	ns
SCL-90-R Psychoticism (D)	ns	ns	ns	ns
SCL-90-R Somatization (D)	ns	ns	NS	ns
SCL-90-R GSI (D)	ns	ns	ns	ns
SCL-90-R PST (D)	p=0.033 (0.72)	ns	ns	ns
SCL-90-R PSDI (D)	ns	ns	p=0.036 (0.43)	NS
WMS-R Verbal Paired Associates (C)[a]	NS	NS	ns	NS
WMS-R Logical Memory, Immediate Recall (C)[a]	NS	NS	ns	NS
WMS-R Logical Memory, Delayed Recall (C)[a]	NS	NS	ns	p=0.039 (0.50)
WMS-R Visual Reproduction, Immediate Recall (C)[a]	NS	NS	ns	NS
WMS-R Visual Reproduction, Delayed Recall (C)[a]	NS	NS	ns	NS

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
        C: Continuous form of dependent variable.
        D: Discrete form of dependent variable.

        The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

        A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

12.4.2   Model 2: Initial Dioxin Analysis

No significant relations were found between initial dioxin and any of the psychological or memory endpoints examined in this chapter. Table 12-26 shows the results of the initial dioxin analysis.

Table 12-26. Summary of Initial Dioxin Analysis (Model 2) for Psychology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Psychoses (D)	NS	ns
Alcohol Dependence (D)	NS	NS
Drug Dependence (D)	--	--
Anxiety (D)	NS	ns
Other Neuroses (D)	NS	ns
Psychology Examination		
SCL-90-R Anxiety (D)	NS	ns
SCL-90-R Depression (D)	NS	ns
SCL-90-R Hostility (D)	NS	NS
SCL-90-R Interpersonal Sensitivity (D)	NS	NS
SCL-90-R Obsessive-compulsive Behavior (D)	NS	NS
SCL-90-R Paranoid Ideation (D)	NS	NS
SCL-90-R Phobic Anxiety (D)	NS	ns
SCL-90-R Psychoticism (D)	NS	NS
SCL-90-R Somatization (D)	NS	NS
SCL-90-R GSI (D)	NS	NS
SCL-90-R PST (D)	NS	ns
SCL-90-R PSDI (D)	NS	NS

Variable	Unadjusted	Adjusted
WMS-R Verbal Paired Associates (C)[a]	ns	ns
WMS-R Logical Memory, Immediate Recall (C)[a]	ns	ns
WMS-R Logical Memory, Delayed Recall (C)[a]	ns	ns
WMS-R Visual Reproduction, Immediate Recall (C)[a]	ns	ns
WMS-R Visual Reproduction, Delayed Recall (C)[a]	NS	NS

[a]A negative slope was considered adverse for this variable.

--: The analysis was not performed because of the sparse number of Ranch Hands with an abnormality.

Note: NS or ns: Not significant (p>0.05).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

      A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

12.4.3 Model 3: Categorized Dioxin Analysis

All significant results for the contrasts of Ranch Hand dioxin categories and Comparisons revealed that Comparisons had a greater prevalence of abnormally high scores on the SCL-90-R subscales. For the SCL-90-R interpersonal sensitivity and PST scales, Comparisons had a significantly greater prevalence of abnormally high scores than Ranch Hands in the low dioxin category and in the low and high dioxin categories combined. For the SCL-90-R paranoid ideation scale, Comparisons had a significantly greater prevalence of abnormally high scores than Ranch Hands in the low and high dioxin categories combined. Table 12-27 presents the results of the categorized dioxin analysis.

Table 12-27. Summary of Categorized Dioxin Analysis (Model 3) for Psychology Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Psychoses (D)	ns	ns	NS	NS
Alcohol Dependence (D)	NS	ns	NS	NS
Drug Dependence (D)	ns	ns	ns	ns
Anxiety (D)	ns	NS	NS	NS
Other Neuroses (D)	p=0.020 (0.75)	NS	p=0.028 (1.43)	p=0.048 (1.27)
Psychology Examination				
SCL-90-R Anxiety (D)	ns	ns	NS	NS
SCL-90-R Depression (D)	ns	ns	NS	NS
SCL-90-R Hostility (D)	ns	ns	NS	ns
SCL-90-R Interpersonal Sensitivity (D)	p=0.034 (0.61)	p=0.010 (0.42)	NS	ns

	UNADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
SCL-90-R Obsessive-compulsive Behavior (D)	ns	ns	NS	ns
SCL-90-R Paranoid Ideation (D)	ns	p=0.032 (0.33)	ns	p=0.047 (0.52)
SCL-90-R Phobic Anxiety (D)	ns	ns	ns	ns
SCL-90-R Psychoticism (D)	ns	p=0.030 (0.51)	NS	ns
SCL-90-R Somatization (D)	ns	ns	NS	ns
SCL-90-R GSI (D)	ns	ns	NS	ns
SCL-90-R PST (D)	ns	p=0.014 (0.49)	NS	ns
SCL-90-R PSDI (D)	ns	ns	NS	NS
WMS-R Verbal Paired Associates (C)[a]	NS	ns	ns	ns
WMS-R Logical Memory, Immediate Recall (C)[a]	NS	NS	ns	ns
WMS-R Logical Memory, Delayed Recall (C)[a]	p=0.027 (0.49)	NS	ns	ns
WMS-R Visual Reproduction, Immediate Recall (C)[a]	NS	ns	ns	ns
WMS-R Visual Reproduction, Delayed Recall (C)[a]	NS	ns	ns	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: NS or ns: Not significant (p>0.05).
   C: Continuous form of dependent variable.
   D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

	ADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Medical Records				
Psychoses (D)	NS	NS	ns	ns
Alcohol Dependence (D)	NS	ns	ns	ns
Drug Dependence (D)	ns	--	--	--
Anxiety (D)	NS	NS	ns	NS
Other Neuroses (D)	ns	NS	NS	NS

Table 12-27. Summary of Categorized Dioxin Analysis (Model 3) for Psychology Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Psychology Examination				
SCL-90-R Anxiety (D)	ns	NS	ns	ns
SCL-90-R Depression (D)	ns	ns	ns	ns
SCL-90-R Hostility (D)	NS	ns	NS	ns
SCL-90-R Interpersonal Sensitivity (D)	ns	p=0.011 (0.40)	ns	p=0.013 (0.56)
SCL-90-R Obsessive-compulsive Behavior (D)	ns	ns	ns	ns
SCL-90-R Paranoid Ideation (D)	ns	ns	ns	p=0.019 (0.45)
SCL-90-R Phobic Anxiety (D)	NS	ns	ns	ns
SCL-90-R Psychoticism (D)	ns	ns	NS	ns
SCL-90-R Somatization (D)	ns	ns	NS	ns
SCL-90-R GSI (D)	ns	ns	ns	ns
SCL-90-R PST (D)	ns	p=0.019 (0.49)	ns	p=0.025 (0.64)
SCL-90-R PSDI (D)	ns	ns	ns	ns
WMS-R Verbal Paired Associates (C)[a]	NS	NS	NS	NS
WMS-R Logical Memory, Immediate Recall (C)[a]	NS	NS	NS	NS
WMS-R Logical Memory, Delayed Recall (C)[a]	NS	NS	NS	NS
WMS-R Visual Reproduction, Immediate Recall (C)[a]	NS	NS	NS	NS
WMS-R Visual Reproduction, Delayed Recall (C)[a]	NS	NS	NS	NS

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

      The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable.

      A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

12.4.4 Model 4: 1987 Dioxin Level Analysis

The only significant relation between 1987 dioxin and any of the psychological or memory endpoints studied occurred with the SCL-90-R phobic anxiety scale. The relation was inverse, however. As 1987 dioxin levels increased, the prevalence of high phobic anxiety scores in Ranch Hands decreased. Table 12-28 displays the results of the 1987 dioxin analysis.

Table 12-28. Summary of 1987 Dioxin Analysis (Model 4) for Psychology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Psychoses (D)	NS	ns
Alcohol Dependence (D)	NS	ns
Drug Dependence (D)	ns	ns
Anxiety (D)	p=0.003 (1.16)	ns
Other Neuroses (D)	p<0.001 (1.19)	NS
Psychology Examination		
SCL-90-R Anxiety (D)	p=0.047 (1.17)	ns
SCL-90-R Depression (D)	NS	ns
SCL-90-R Hostility (D)	NS	ns
SCL-90-R Interpersonal Sensitivity (D)	NS	ns
SCL-90-R Obsessive-compulsive Behavior (D)	p=0.043 (1.13)	ns
SCL-90-R Paranoid Ideation (D)	NS	ns
SCL-90-R Phobic Anxiety (D)	NS	p=0.014 (0.80)
SCL-90-R Psychoticism (D)	NS	NS
SCL-90-R Somatization (D)	p=0.015 (1.17)	NS
SCL-90-R GSI (D)	p=0.040 (1.16)	ns
SCL-90-R PST (D)	NS	ns
SCL-90-R PSDI (D)	p=0.016 (1.23)	NS
WMS-R Verbal Paired Associates (C)[a]	p=0.020 (-0.168)	ns
WMS-R Logical Memory, Immediate Recall (C)[a]	p=0.001 (-0.237)	ns
WMS-R Logical Memory, Delayed Recall (C)[a]	p=0.004 (-0.237)	ns
WMS-R Visual Reproduction, Immediate Recall (C)[a]	ns	ns
WMS-R Visual Reproduction, Delayed Recall (C)[a]	ns	ns

[a]A negative slope was considered adverse for this variable.

Note: NS or ns: Not significant (p>0.05).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

12.4.5 Summary of Significant Results

Table 12-29 summarizes the significant results (p≤0.05) for the adjusted analyses that were performed for the psychology assessment. The dependent variable and its table reference are listed along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and is explained in footnotes.

Table 12-29. Summary of Results from Significant Adjusted Analyses in the Psychology Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Other Neuroses (12-7)	1	RH vs. C, Officer	0.043	0.73 (0.54,0.99)	RH: 43.5% C: 51.5%	(a)
SCL-90-R Interpersonal Sensitivity (12-11)	1	RH vs. C, All	0.013	0.65 (0.46,0.92)	RH: 7.4% C: 10.7%	(a)
	1	RH vs. C, Officer	0.045	0.47 (0.23,0.98)	RH: 3.3% C: 6.7%	(a)
	3	Low RH vs. C	0.011	0.40 (0.20,0.81)	RH: 4.8% C: 10.7%	(b)
	3	Low plus High RH vs. C	0.013	0.56 (0.36,0.88)	RH: 7.9% C: 10.7%	(b)
SCL-90-R Paranoid Ideation (12-13)	1	RH vs. C, All	0.011	0.53 (0.32,0.88)	RH: 3.1% C: 5.6%	(a)
	1	RH vs. C, Enlisted Groundcrew	0.033	0.51 (0.27,0.95)	RH: 4.8% C: 8.8%	(a)
	3	Low plus High RH vs. C	0.019	0.45 (0.23,0.88)	RH: 3.3% C: 5.6%	(b)
SCL-90-R Phobic Anxiety (12-14)	4	All RH: 1987 Dioxin	0.014	0.80 (0.66,0.96)	Low: 6.9% Medium: 5.4% High: 9.1%	(c)
SCL-90-R PST (12-18)	1	RH vs. C, All	0.033	0.72 (0.53,0.98)	RH: 9.6% C: 12.6%	(a)
	3	Low RH vs. C	0.019	0.49 (0.27,0.89)	RH: 6.7% C: 12.6%	(b)
	3	Low plus High RH vs. C	0.025	0.64 (0.43,0.94)	RH: 10.5% C: 12.6%	(b)
SCL-90-R PSDI (12-19)	1	RH vs. C, Enlisted Flyer	0.036	0.43 (0.20,0.95)	RH: 7.5% C: 15.1%	(a)
WMS-R Logical Memory, Delayed Recall (12-22)[a]	1	RH vs. C, Enlisted Groundcrew	0.039	0.50 (0.02,0.97)	RH: 8.46 C: 7.97	(d)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

(d): Continuous variable: difference of adjusted means and 95% confidence interval was presented; adjusted means were presented for each exposure group in contrast.

[a]A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: RH = Ranch Hand.
        C = Comparison.

        Model 3:   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
                     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
                     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

        Model 4:   Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

12.5   CONCLUSION

Five psychological disorders, which were verified by a medical records review, 12 measures from the SCL-90-R inventory, and 5 tests from the WMS-R, were examined in the psychology assessment. The SCL-90-R consisted of nine primary symptom dimensions and three broad indices of psychological distress.

More Comparisons than Ranch Hands had high scores on the SCL-90-R interpersonal sensitivity, paranoid ideation, and PST scales. Significant results within the three occupational stratum showed that more Comparisons than Ranch Hands had a history of other neuroses and high scores on the SCL-90-R interpersonal sensitivity, PSDI, and paranoid ideation scale. Comparison enlisted groundcrew had a lower mean score on the delayed recall portion of the WMS-R Logical Memory test than Ranch Hand enlisted groundcrew.

No significant relations were found between initial dioxin and any of the psychological or memory endpoints examined in this chapter. A significant inverse relation between 1987 dioxin and the SCL-90-R phobic anxiety scale was found.

Ranch Hands had a smaller percentage of abnormally high scores on the SCL-90-R interpersonal sensitivity, paranoid ideation, and PST scales. Ranch Hand enlisted groundcrew had an increased mean score on the delayed recall portion of the WMS-R Logical Memory test. The percentage of abnormally high scores on the SCL-90-R phobic anxiety scale score decreased with increased 1987 dioxin levels. None of the memory functioning and psychopathology scales were adversely associated with exposure to herbicides or dioxin.

REFERENCES

1. Derogatis, L.R. 1975. The SCL-90-R. Clinical Psychometrics Research: Baltimore, MD.

2. Wechsler, D., and C. Stone. Wechsler Memory Scale-Revised. The Psychological Corporation: San Antonio, TX.

3. Peterson, R.E., M.D. Seefeld, B.J. Christian, C.L. Potter, C.K. Kelling, and R.E. Keesey. 1984. The wasting syndrome in 2,3,7,8-tetrachlorodibenzo-p-dioxin toxicity: Basic features and their interpretation. In: Banbury Report 18: Biological Mechanisms of Dioxin Action. A. Poland and R.D. Kimbrough, eds. Cold Spring Harbor Laboratory: Cold Spring Harbor, NY.

4. Piper, W.N., J.Q. Rose, and P.J. Gehring. 1973. Excretion and tissue distribution of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the rat. *Environmental Health Perspectives* 5:241-4.

5. Gasiewicz, T.A., L.E. Geiger, G. Rucci, and R.A. Neal. 1983. Distribution, excretion, and metabolism of 2,3,7,8-tetrachlorodibenzo-p-dioxin in C57BL/6J, DBA/2J, and B6D2F1/J mice. *Drug Metabolism and Disposition* 11:397-403.

6. Abraham, K., T. Weismüller, H. Hagenmaier, and D. Neubert. 1990. Distribution of PCDDs and PCDFs in various tissues of marmoset monkeys. *Chemosphere* 20:1071-8.

7. Sirkka, U., S.A. Nieminen, R. Pohjanvirta, J. Tuomisto, and P. Ylitalo. 1990. Behavioral effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in rats. *European Journal of Pharmacology* 183:1517.

8. Sirkka, U., R. Pohjanvirta, S.A. Nieminen, J. Tuomisto, and P. Ylitalo. 1992. Acute neurobehavioral effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in rats. *Pharmacology and Toxicology* 71:284-8.

9. Widholm, J.J., B.W. Seo, B.J. Strupp, R.F. Seegal, and S.L. Schantz. 2003. Effects of perinatal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin on spatial and visual reversal learning in rats. *Neurotoxicology and Teratology* 25:459-71.

10. B.W. Seo, B.E. Powers, J.J. Widholm, and S.L. Schantz. 2000. Radial arm maze performance in rats following gestational and lactational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Neurotoxicology and Teratology* 22:511-9.

11. Widholm, J.J., B.W. Seo, B.J. Strupp, R.F. Seegal, and S.L. Schantz. 2003. Effects of perinatal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin on spatial and visual reversal learning in rats. *Neurotoxicology and Teratology* 25:459-71.

12. Bowman, R.E., S.L. Schantz, M.L. Gross, and S.A. Ferguson. 1989. Behavioral effects in monkeys exposed to 2,3,7,8-TCDD transmitted maternally during gestation and for four months of nursing. *Chemosphere* 18:235-42.

13. Bowman, R.E., S.L. Schantz, and S.A. Ferguson. 1990. Controlled exposure of female rhesus monkeys to 2,3,7,8-TCDD: Cognitive behavioral effects in their offspring. *Chemosphere* 20:1103-8.

14. Schantz, S.L., and R.E. Bowman. 1989. Learning in monkeys exposed perinatally to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Neurotoxicology and Teratology* 11:13-9.

15. Schantz, S., S. Ferguson, and R. Bowman. 1992. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on behavior of monkeys in peer groups. *Neurotoxicology and Teratology* 14(6):433-46.

16. Hoffman, R.E., P.A. Stehr-Green, K.B. Webb, R.G. Evans, A.P. Knutsen, W.F. Schramm, B.B. Gibson, and K.K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *The Journal of the American Medical Association* 225:2031-8.

17. Stehr-Green, P. A., R. Hoffman, K. Webb, R. G. Evans, A. Knutsen, W. Schramm, J. Staake, B. Gibson, and K. Steinberg. 1987. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Chemosphere* 16:2089-94.

18. Peper, M., M. Klett, R. Frentzel-Beyme, and W.D. Heller. 1993. Neuropsychological effects of chronic exposure to environmental dioxins and furans. *Environmental Research* 60:124-35.

19. Wechsler, D. 1972. Wechsler Adult Intelligence Scale. The Psychological Corporation: New York, NY.

20. Suskind, R.R. 1953. A clinical and environmental survey. In: Report of the Kettering Laboratory. Monsanto Chemical Company: Nitro, WV.

21. Ashe, W.F, and R.R. Suskind. 1949, 1950. Reports on chloracne cases. In: Report of the Kettering Laboratory. Monsanto Chemical Company: Nitro, WV.

22. Moses, M., R. Lilis, K.D. Crow, J. Thornton, A. Fischbein, H.A. Anderson, and I.J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *American Journal of Industrial Medicine* 5:161-82.

23. Suskind, R.R., and V.S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *The Journal of the American Medical Association* 251:2372-80.

24. Baader, E.W., and A.J. Bauer. 1951. Industrial intoxication due to pentachlorophenol. *Industrial Medicine and Surgery* 20:289-90.

25. Suskind, R.R. 1977. Chloracne and associated health problems in the manufacture of 2,4,5-T. Report to the Joint Conference, National Institute of Environmental Health Sciences and International Agency for Research on Cancer, World Health Organization, January, Lyon, France.

26. Vos, J.G., T.J. Sterringa, D. Zellenrath, H.J. Docter, and L.M. Daldkerup. 1977. TCDD accident at a chemical factory in the Netherlands. Report to the Joint Conference, National Institute of Environmental Health Sciences and International Agency for Research on Cancer, World Health Organization, January, Lyon, France.

27. Pazderova-Vejlupkova, J., M. Nemcova, J. Pickova, L. Jirasek, and E. Lukás. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Archives of Environmental Health* 36:5-11.

28. Poland, A.P., D. Smith, G. Metter, and P. Possick. 1971. A health survey of workers in a 2,4-D and 2,4,5-T plant, with special attention to chloracne, porphyria cutanea tarda, and psychologic parameters. *Archives of Environmental Health* 22:316-27.

29. Oliver, R.M. 1975. Toxic effects of 2,3,7,8-tetrachlorodibenzo-1,4-dioxin in laboratory workers. *British Journal of Industrial Medicine* 32:46-53.

30. Hathaway, S.R., and J.C. McKinley. 1940. The Minnesota Multiphasic Personality Inventory. The Psychological Corporation: New York, NY.

31. Wechsler, D. 1981. Wechsler Adult Intelligence Scale-Revised. The Psychological Corporation: San Antonio, TX.

32. Benton, A.L. 1955. The Revised Visual Retention Test: Clinical and experimental applications. Psychological Corporation: New York, NY.

33. Pelclová, D., Z. Fenclová, Z. Dlaskova, P. Urban, E. Lukás, B. Procházka, C. Rappe, J. Preiss, A. Kocan, and J. Vejlupkova. 2001. Biochemical, neuropsychological, and neurological abnormalities following 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure. *Archives of Environmental Health* 56:493-500.

34. Pelclová, D., Z. Fenclová, J. Preiss, B. Procházka, J. Spácil, Z. Dubská, B. Okrouhlík, E. Lukás, and P. Urban. Lipid metabolism and neuropsychological follow-up study of workers exposed to 2,3,7,8- tetrachlorodibenzo-p-dioxin. *International Archives of Occupational and Environmental Health* 75 Suppl 1:60-6.

35. Alderfer, R., M. Sweeney, M. Fingerhut, R. Hornung, K. Wille, and A. Fidler. 1992. Measures of depressed mood in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Chemosphere* 25:247-50.

36. Zober A., M.G. Ott, and P. Messerer. 1994. Morbidity follow up study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

37. Robinowitz, R., W.R. Roberts, M.P. Dolan, E.T. Patterson, H.L. Charles, H.G. Atkins, and W.E. Penk. 1989. Carcinogenicity and teratogenicity vs. psychogenicity: Psychological characteristics associated with self-reported Agent Orange exposure among Vietnam combat veterans who seek treatment for substance abuse. *Journal of Clinical Psychology* 45:718-28.

38. Decoufle, P., P. Holmgreen, C.A. Boyle, and N.E. Stroup. 1992. Self-reported health status of Vietnam veterans in relation to perceived exposure to herbicides and combat. *American Journal of Epidemiology* 135:312-23.

39. U. S. Centers for Disease Control. 1988. Health status of Vietnam veterans. In: Part 1, Psychosocial Characteristics. *The Journal of the American Medical Association* 259:2701-2.

40. Barrett, D.H., R.D. Morris, F.Z. Akhtar, and J.E. Michalek. 2001. Serum dioxin and cognitive functioning among veterans of Operation Ranch Hand. *Neurotoxicology* 22:491-502.

41. Michalek, J.E., B.R. Burnham, H.E. Marden, Jr., J.N. Robinson, V.V. Elequin, J.C. Miner, R.W. Ogershok, W.K. Sneddon, W.D. Grubbs, B.C. Cooper, R.G. Land, V.K. Rocconi, M.E. Yeager, D.E. Williams, and M.E.B. Owens. 2000. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1997 follow-up examination results. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

42. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline morbidity study results. NTIS: AD A 138-340. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

43. Lathrop, G.D., S.G. Machado, T.G. Karrison, W.D. Grubbs, W.F. Thomas, W.H. Wolfe, J.E. Michalek, J.C. Miner, and M.R. Peterson. 1987. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188262. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

44. Thomas, W.F., W.D. Grubbs, T.G. Karrison, M.B. Lustik, R.H. Roegner, D.E. Williams, W.H. Wolfe, J.E. Michalek, J.C. Miner, and R.W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: I. 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. USAF School of Aerospace Medicine, Human Systems Division (AFSC), Brooks Air Force Base, TX.

45. Michalek, J.E, D.H. Barrett, R.D. Morris, and W.G. Jackson, Jr. 2003. Serum dioxin and psychological functioning in U.S. Air Force veterans of the Vietnam War. *Military Medicine* 168:153-9.

46. Kim J.S., H.S. Lim, S.I. Cho, H.K. Cheong, and M.K. Lim. 2003. Impact of Agent Orange exposure among Korean Vietnam veterans. *Industrial Health* 41:149-157.

47. Boll, T.J. 1981. The Halstead-Reitan Neuropsychological Test Battery. In: Handbook of Clinical Neuropsychology. S.B. Filskov, and T.J. Boll, eds. John Wiley & Sons: New York, NY.

48. Jastak, J.F., S.W. Bijou, and S.R. Jastak. 1978. Wide Range Achievement Test. Jastak Associates: Wilmington, DE.

49. Millon, T. 1984. Millon Clinical Multiaxial Inventory Manual. Interpretive Scoring Systems: Minneapolis, MN.

50. Institute of Medicine. 2003. Veterans and Agent Orange: Update 2002. National Academy Press: Washington, DC.

51. Weider, A., H.G. Wolff, K. Brodman, B. Mittelman, and D. Wechsler. 1946 (rev. 1949). Cornell Index. The Psychological Corporation: New York, NY.

52. Brodman, K., A.J. Erdmann, Jr., H.G. Wolff. 1949 (rev. 1986). Cornell Medical Index—Manual and Questionnaires. Cornell University Medical College: New York, NY.

53. Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L. R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

54. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57:369-78.

55. Tulsky, D., J. Zhu, and M.F. Ledbetter. 2002. WAIS-III/WMS-III technical manual. Psychological Corporation: San Antonio, TX.

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13 GASTROINTESTINAL ASSESSMENT

13.1 INTRODUCTION

13.1.1 Background

13.1.1.1 Organs/Diseases

The following seven categories, based on self-reporting by participants, were evaluated as part of the gastrointestinal assessment in the Air Force Health Study (AFHS): uncharacterized hepatitis, jaundice, alcohol-related chronic liver disease and cirrhosis, chronic liver disease and cirrhosis not related to alcohol, liver abscess and sequelae of chronic liver disease, enlarged liver (hepatomegaly), and other disorders of the liver. The self-reported data were verified by a medical records review. Current hepatomegaly was determined at the 2002 physical examination. The AFHS gastrointestinal assessment also included an evaluation of laboratory data of 28 measurements, which included the following: aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyltransferase (GGT), alkaline phosphatase, total bilirubin, direct bilirubin, lactate dehydrogenase (LDH), cholesterol, high-density lipoprotein (HDL) cholesterol, the ratio of cholesterol to HDL cholesterol, triglycerides, creatine phosphokinase, serum amylase, antibodies for hepatitis A, serological evidence of prior hepatitis B infection, antibodies for hepatitis C, stool hemoccult, prothrombin time, and 10 components in a protein profile.

Several factors have been studied that can affect lipid levels or are associated with liver disease, including diet, genetic makeup, acute or chronic illness, diabetes, and obesity. Important determinants of liver disease include excessive alcohol ingestion and chronic viral infection, while peptic ulcer disease is associated with bacterial infection and genetic predisposition (1). The occurrence of ulcers had been investigated for the analyses of the 1985 and 1987 AFHS follow-up examinations. The results were nonsignificant in these analyses, however, and analysis of ulcers was not performed for the 1992, 1997, or 2002 follow-up examination reports.

13.1.1.2 Toxicology

The digestive system, particularly the liver (2-8) and stomach (3, 9-13), were clearly defined as target organs for dioxin toxicity in laboratory animals. Dioxin ingested by rodents (14-19) and adult monkeys (20) is absorbed by the intestinal lymphatics, transported by chylomicrons in the enterohepatic circulation, and preferentially stored in adipose tissue and the liver. Hepatotoxic manifestations, which appear to be dose- and time-dependent, include cellular hypertrophy, parenchymal necrosis (principally centrilobular), fatty degeneration, and the production of altered hepatic foci, a microscopic precursor in hepatic carcinogenesis (7, 21-23). Gastric endpoints were the subject of several reports focused on histologic changes (3, 11, 12, 24) and endocrine secretory abnormalities (e.g., hypergastrinemia and hypothyroxinemia) (9, 10, 25) associated with dioxin toxicity.

Many hepatic biochemical reactions related to dioxin toxicity were studied in rats, including lipid peroxidation (26-34), hepatic prostaglandin synthase activity (35, 36), liver ethoxyresorufin O-deethylase activity (37), and inhibition of glutathione peroxidase (27, 38, 39). Results from several lines of biochemical investigation created a bridge between animal and human studies, including research into lipid (30, 40, 41) and porphyrin metabolism (42-44). In rats, dioxin has been shown to increase the

activity of glucuronyl transferase (45), an observation that led to the use of urinary d-glucaric acid as a marker for dioxin exposure in several human epidemiologic studies (46-50). Direct effects of dioxin on gastrointestinal organs other than the liver have not been observed, and human data are lacking to evaluate whether and how subjects exposed to dioxin have a modified lipoprotein metabolism (1).

In two case reports of extreme phenoxyherbicide toxicity by ingestion in three workers, effects included coma, rhabdomyolysis, and renal failure rather than effect on the digestive system (51, 52). Recently, a case study of two workers with severe dioxin intoxication found moderately elevated levels of blood lipids (triglycerides and cholesterol) in one worker and normal levels in the other relative to those generally seen in unexposed persons (53).

13.1.1.3 Epidemiology: Blood Chemistry Levels

Studies of exposure to dioxin resulting from industrial accidents or point-source contamination in the environment generally found little evidence for an effect of dioxin exposure on blood chemistry levels. The 1976 chemical explosion in Seveso, Italy, resulted in several reports on the exposed residents (54-57). In one study, 152 subjects with chloracne, a marker for high-level dioxin exposure, were compared with 123 age- and gender-matched controls from nearby towns. None of the serum biochemistry indices, such as GGT, triglycerides, and cholesterol, showed substantial differences between exposed and unexposed subjects (54). Other studies of the Seveso population reached similar conclusions (48, 49, 55, 56, 58, 59).

The relation between point-source environmental exposure to dioxin and levels of lipids and liver enzymes has been the focus of a limited number of epidemiologic studies. In 1971, waste byproducts contaminated with dioxin were mixed with oils and widely sprayed for dust control in residential areas in eastern Missouri. Two studies were conducted: one at Quail Run, Missouri, in 1984-85 (47) and the other at Times Beach, Missouri, in 1983 (60). No effects of dioxin exposure on lipid levels were seen among 154 exposed and 155 unexposed persons at Quail Run (47); however, a positive association of unknown clinical relevance was observed between liver enzyme levels (AST, ALT, GGT, alkaline phosphatase, and alanine aminopeptidase) and years of exposure in this population (47). No indication for hepatic enzyme elevations or increased lipid levels in association with adipose dioxin levels in the Times Beach population was found (60, 61).

Although numerous occupational studies reported on lipid levels and liver enzymes associated with dioxin exposure (46, 51-53, 62-73), these studies did not all use the same clinical measures or report similar outcomes. Elevated levels of GGT and triglycerides were observed among workers with chloracne relative to those without chloracne in a study population of 226 employees exposed to dioxin during the manufacturing of trichlorophenol (64). Another follow-up study of 55 dioxin-exposed workers in the same industry reported that more than half the workers suffered from hyperlipemia and hypercholesterolemia and 20 percent of the subjects were found to have hepatic lesions (66).

The epidemiologic study conducted by the National Institute of Occupational Safety and Health (NIOSH) is one of several occupational studies relating serum dioxin levels to serum lipid and liver enzyme concentrations (46, 63). No association between dioxin exposure and out-of-normal-range liver enzyme concentrations other than GGT was found. This relation with GGT, however, was limited to exposed workers with a history of substantial alcohol consumption and did not appear to be directly related to the body burden of dioxin (46). In contrast, some indication for a positive association between serum dioxin levels and concentrations of triglyceride and HDL was found (63).

Various blood chemistry measures were associated with dioxin exposure in other occupational studies. Elevated levels of the liver enzyme GGT provide some evidence for the hepatic effects of dioxin exposure during the manufacturing of the herbicide 2,4,5-T, as found in a study of 159 cases of chloracne relative to worker controls (65). Hyperlipidemia was associated with serum dioxin levels among 96 Japanese workers exposed to dioxins in emission gases from municipal waste incinerators (74). A small study of 13 workers involved in herbicide production in the Czech Republic revealed positive correlations between serum dioxin levels and concentrations of cholesterol, triglycerides, and plasma lipids and beta-lipoproteins (67, 71).

Recently, a study of 133 municipal waste incinerator workers found cholesterol levels to be elevated in workers with high blood dioxin levels as compared to workers with low exposure (72). Some indication of elevated liver enzyme concentrations (AST, ALT, total bilirubin, and triglycerides) and the risk of fatty liver existed, but results were not statistically significant (72). A recent study of 96 Japanese municipal incinerator workers chronically exposed to dioxins, however, did not find a correlation between blood dioxin levels and blood chemistry parameters (73). Other occupational studies also found little evidence for an association between levels of hepatic enzymes and serum dioxin (68-70, 75).

Several reports of Vietnam veterans focused on the potential association of hepatic dysfunction with dioxin exposure (76-81). In one retrospective cohort study of 100 Vietnam veterans, job classification, self-reported herbicide use, and duration of exposure were used as surrogates for exposure to Agent Orange. Liver abnormalities in the form of elevated ALT, AST, or alkaline phosphatase levels were shown to be related only to the duration of exposure, which was attributed to alcoholism and viral hepatitis rather than Agent Orange exposure (79). In the 1987 follow-up examination of Ranch Hand personnel in the AFHS, the risk of an abnormal level of triglycerides was slightly elevated among 995 Ranch Hands relative to 1,299 Comparison subjects (78). More recently, serum dioxin levels measured in 1987 and 1992 were compared with indicators of gastrointestinal abnormalities among Ranch Hands with follow-up examinations in 1982, 1985, 1987, and 1992. Based on liver function test results obtained in 1992, levels of ALT and GGT were positively associated with serum dioxin levels in a dose-response fashion. Similar results were reported for the 1997 follow-up examination (81); however, the plausibility of these associations has been questioned (77).

In a 1994 report published by the Institute of Medicine (IOM), the committee concluded that there is "inadequate or insufficient" evidence of an association between exposure to dioxin and changes in hepatic enzymes or lipid abnormalities (82). This conclusion remained unaltered in the 2002 IOM report (1).

13.1.1.4 Epidemiology: Gastrointestinal Diseases

The Seveso studies found little indication of an increased risk of digestive diseases. A recent follow-up study of the Seveso population, comprising approximately 6,700 residents with high exposure and more than 200,000 unexposed controls, found little evidence for an increased risk of mortality from nonmalignant digestive diseases (57, 83).

A number of occupational cohort studies were conducted to evaluate the mortality and morbidity experience among workers exposed to dioxin (46, 70, 84-89). In the NIOSH study (46), no increased risk of hepatic and gastrointestinal disease was found among 281 exposed workers as compared to 260 unexposed controls. In addition, no evidence of an increased mortality risk of nonmalignant digestive system diseases was found among 549 Dutch workers (84) and 21,863 other European workers in 12 countries exposed to dioxin in the production of phenoxy herbicides (86, 89). Although a substantially increased risk of mortality from gastric and duodenal ulcer was reported in a cohort of 770 workers with potential pentachlorophenol exposure, the number of observed cases was too small to establish an

association with dioxin exposure (88). In a cohort of 243 workers exposed to dioxin after a chemical accident at the trichlorophenol unit of a BASF chemical facility, little evidence for a positive association between lipid dioxin levels and mortality from digestive system diseases was found (87). In an earlier morbidity study of the same cohort, the rates of illness episodes of gastrointestinal diseases were similar between dioxin-exposed workers and unexposed referents; however, the rate of chronic liver disease was slightly increased among those with high dioxin exposure (70).

The evidence for an association between serum dioxin levels and gastrointestinal disease among Ranch Hand personnel in the AFHS was reported (76-78, 80, 81). In the 1987 follow-up examination, some indication of an increased risk was found for "not alcohol-related chronic liver disease and cirrhosis" and "other liver conditions" among Ranch Hands as compared to the control population (78). Among 1,261 Ranch Hands followed through 1993, an increased risk of digestive disease mortality (n=9) was found compared to the mortality experience of veterans who were not involved in spraying herbicides in Vietnam (76). These analyses were not adjusted for alcohol consumption. Recently, an increased risk of "other liver disorders" was observed among Ranch Hand veterans with the highest dioxin levels, but the interpretation was uncertain (77, 81). Some indication of an increased risk of mortality from digestive system diseases was found in other studies of Vietnam veterans, but indicators of dioxin exposure were not evaluated (90, 91).

In their reports, the IOM committees concluded that there is "inadequate or insufficient" evidence for an association between exposure to dioxin and gastrointestinal and digestive diseases (1, 82, 92-94).

13.1.2 Summary of Previous Analyses of the Air Force Health Study

13.1.2.1 1982 Baseline Examination Summary Results

The 1982 AFHS examination included an extensive evaluation of hepatic status by questionnaire, physical examination, and laboratory testing. The questionnaire elicited data on liver conditions, liver disease, and symptoms compatible with porphyria cutanea tarda (PCT), as well as detailed information on PCT risk factors (e.g., alcohol consumption, chemical exposures). The physical examination measured hepatomegaly, or enlarged liver, when present and determined liver function and porphyrin patterns using a comprehensive battery of 12 laboratory tests.

The questionnaire showed that Ranch Hands reported more miscellaneous liver conditions (verified by a medical records review) and more skin changes compatible with PCT than their Comparisons. Although the reported skin changes were statistically significant, no cases of PCT were diagnosed at examination in either cohort.

Ranch Hands had significantly higher GGT and LDH means and lower cholesterol means; no differences were found for bilirubin or alkaline phosphatase means. There were no significant group differences in uroporphyrin, coproporphyrin, or d-aminolevulinic acid levels, nor did any test set support a diagnosis of PCT.

A comprehensive hepatic evaluation did not reveal any consistent pattern of significant liver damage in the Ranch Hand group.

13.1.2.2 1985 Follow-up Examination Summary Results

The 1985 AFHS examination continued the emphasis on gastrointestinal function and expanded the porphyrin test battery to six assays. The interval questionnaire revealed sparse reporting of liver disorders

from 1982 to 1985. Reported liver diseases were verified by medical records, and these data were added to the verified baseline history to assess possible lifetime differences. No significant differences were found.

Emphasis was placed on nine laboratory test variables measuring liver functions: AST, ALT, GGT, alkaline phosphatase, total bilirubin, direct bilirubin, LDH, cholesterol, and triglycerides. In addition, uroporphyrin and coproporphyrin measurements were obtained to assess the likelihood of PCT.

The results showed a significantly lower mean ALT level, a greater mean alkaline phosphatase level, and a lower mean uroporphyrin level.

Overall, the 1985 follow-up examination laboratory data showed no adverse clinical or exposure patterns. The continuous statistical tests detected significant mean shifts that were not mirrored by the discrete tests. These findings were generally consistent with the 1982 baseline examination data.

Interval reporting of PCT-like symptoms of skin patches, bruises, and sensitivity was significantly increased in Ranch Hands. When these historic data were contrasted to both uroporphyrin and coproporphyrin abnormalities, no correlation was apparent, nor were there any significant group differences. The likelihood of actual PCT among Ranch Hands appeared to be remote.

13.1.2.3 1987 Follow-up Examination Summary Results

Overall, the gastrointestinal assessment did not find the health of the Ranch Hand group to be significantly different from that of the Comparison group. Group differences based on verified historical data from the questionnaire were not significant for eight categories of liver disease. No significant group difference was found for past or present occurrence of peptic ulcers. The prevalence of hepatomegaly diagnosed at the physical examination also was not significantly different between the two groups. The only significant finding from the laboratory examination variables was that Ranch Hands had a higher mean alkaline phosphatase than Comparisons, also noted at the 1985 follow-up examination. Group differences for the other laboratory variables (AST, ALT, GGT, total bilirubin, direct bilirubin, LDH, cholesterol, HDL, cholesterol-HDL ratio, triglycerides, and creatine phosphokinase) were not significant.

13.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Examination Results

The serum dioxin analysis of the 1987 follow-up examination results did not show a significant association with any of the verified historical liver disorder variables. The analyses of the laboratory variables detected significant associations between dioxin (1987 and estimated initial) and lipid-related health indices such as cholesterol, HDL cholesterol, the cholesterol-HDL ratio, and triglycerides. These findings were consistent with significant associations seen for fat-related variables in other clinical assessments, such as the body fat results in the general health assessment and the diabetes and glucose results noted in the endocrinology assessment, and may represent a dioxin-mediated alteration of biochemical processes.

13.1.2.5 1992 Follow-up Examination Summary Results

The gastrointestinal assessment found isolated significant differences between Ranch Hands and Comparisons, but overall, the health of the two groups did not differ substantially. The serum dioxin analyses indicated that estimated initial dioxin generally was not associated with historical liver disorders or current laboratory measurements. The analyses did reveal that 1987 dioxin levels were often highly associated with lipid-related health indices, such as cholesterol, HDL cholesterol, the cholesterol-HDL

ratio, and triglycerides, as well as with some of the hepatic enzymes (ALT and GGT) and proteins. These seemingly discordant results may have been explained in part because the initial dioxin analyses adjusted for differential half-life elimination related to body fat, while no adjustment was made in the analyses of 1987 dioxin. These significant findings may have been the result of a subclinical dioxin effect on lipid metabolism.

13.1.2.6 1997 Follow-up Examination Summary Results

The gastrointestinal assessment was based on eight disorders as determined from a review and verification of each participant's medical records, a physical examination determination of hepatomegaly, and 29 laboratory measurements or indices. The laboratory parameters included measurements of hepatic enzyme activity, hepatobiliary function, lipid and carbohydrate indices, and a protein profile. In addition, the presence of hepatitis and fecal occult blood was investigated.

Analyses of Ranch Hands versus Comparisons showed higher mean levels of alkaline phosphatase, α-1-antitrypsin, and haptoglobin in Ranch Hands than in Comparisons. In addition, significantly more Ranch Hands than Comparisons had high haptoglobin levels. A review of medical records showed a positive association between other liver disorders and initial dioxin. Twelve percent of the participants with the other liver disorders condition had nonspecific laboratory test elevations. A significant association between initial dioxin and high levels of AST also was revealed.

Analyses of categorized dioxin revealed a significantly higher percentage of other liver disorders among Ranch Hands in the high dioxin category than among Comparisons. Higher mean levels of GGT, triglycerides, and α-1-antitrypsin were observed in Ranch Hands in the high dioxin category than in Comparisons. Ranch Hands in the high dioxin category had a greater prevalence of abnormal AST, triglyceride, and prealbumin levels than did Comparisons.

Many significant associations between the laboratory examination variables and 1987 dioxin levels were observed. In both the continuous and discrete forms, the hepatic enzymes ALT, AST, and GGT revealed significant positive associations with 1987 dioxin. In addition, significant positive associations between 1987 dioxin and the cholesterol-HDL ratio, triglycerides, and creatine phosphokinase were present.

In summary, the analysis of the 1997 follow-up examination data reflected patterns that have been observed and documented in prior examinations. The composite category of disease named "other liver disorders" exhibited a dose-response relation with dioxin. Isolated group differences exist, but 1987 dioxin levels were strongly related to hepatic enzymes such as AST, ALT, and GGT, and to lipid-related health indices such as cholesterol, HDL, and triglycerides. These results were consistent with a dose-response effect and may be related to unknown subclinical effects of dioxin. Although hepatic enzymes showed an association with dioxin, there was no evidence of an increase in overt liver disease.

13.1.3 Parameters for the 2002 Gastrointestinal Assessment

13.1.3.1 Dependent Variables

Questionnaire, physical examination, and laboratory data were used in the gastrointestinal assessment. The questionnaire data were organized by ICD-9-CM medical coding categories.

13.1.3.1.1   Medical Records Variables

During the 2002 health interview, each study participant was asked about the occurrence of hepatitis, jaundice, cirrhosis, enlarged liver, and other liver conditions. Medical records review was accomplished to confirm reported problems for these conditions and to identify any unreported liver conditions for each participant that attended the 2002 physical examination. These data from the 2002 physical examination were combined with data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations to form a complete history of liver conditions for each participant. The analyses performed in this chapter were based on the 1,951 participants who attended the 2002 follow-up examination.

The verified results were grouped into the following seven categories of disorders for analysis: (1) uncharacterized hepatitis (non-A, non-B, and non-C), (2) jaundice (unspecified, not of the newborn), (3) chronic liver disease and cirrhosis (alcohol-related), (4) chronic liver disease and cirrhosis (nonalcohol-related), (5) liver abscess and sequelae of chronic liver disease, (6) enlarged liver (hepatomegaly), and (7) other disorders of the liver. The purpose of the uncharacterized hepatitis (non-A, non-B, and non-C) category was to define a category that was neither clearly A nor B nor C, so that liver disease misdiagnosed as "viral hepatitis" could be detected. This approach to historical hepatitis created a group of cases that could have been chemically induced. The following ICD-9-CM codes were used for these disorders: uncharacterized hepatitis (ICD-9-CM codes 70.49, 70.59, 70.6, 70.9, 571.40, 571.41, 571.49, and 573.3), jaundice (ICD-9-CM code 782.4), alcohol-related chronic liver disease and cirrhosis (ICD-9-CM codes 571.0-571.3), nonalcohol-related chronic liver disease and cirrhosis (ICD-9-CM codes 571.40–571.9), liver abscess and sequelae of chronic liver disease (ICD-9-CM codes 572.0–572.8), enlarged liver (ICD-9-CM code 789.1), and other disorders of the liver (ICD-9-CM codes 573.0–573.9, 790.4, 790.5, and 794.8). An analysis of the history of acute and subacute necrosis of the liver (ICD-9-CM code 570) also was planned, but no occurrences were found in this population.

For each condition under study, participants with a pre-Southeast Asia (SEA) diagnosis were excluded from the analysis. In addition, the analysis of alcohol-related chronic liver disease and cirrhosis excluded participants with zero lifetime alcohol history because nondrinkers would not be at risk for alcohol-related liver disease.

13.1.3.1.2   Physical Examination Variable

One variable from the 2002 physical examination, current hepatomegaly, was analyzed in the gastrointestinal assessment. This variable was coded as "yes" or "no." Participants whose blood contained hepatitis B surface antigen (HBsAg) or hepatitis C antibodies were excluded from the analysis of current hepatomegaly to account for the effects of these viruses on chronic hepatic disease.

13.1.3.1.3   Laboratory Variables

The 2002 examination emphasized the evaluation of laboratory data through the analysis of 28 measurements. These laboratory variables were AST (U/L), ALT (U/L), GGT (U/L), alkaline phosphatase (U/L), total bilirubin (mg/dL), direct bilirubin (mg/dL), LDH (U/L), cholesterol (mg/dL), HDL cholesterol (mg/dL), cholesterol-HDL ratio, triglycerides (mg/dL), creatine phosphokinase (U/L), serum amylase (U/L), antibodies for hepatitis A, serological evidence of prior hepatitis B infection (positive anti-HBsAg or positive hepatitis B core antibody), antibodies for hepatitis C, stool hemoccult, prothrombin time (seconds), and 10 components (in mg/dL) in a protein profile (prealbumin, albumin, α-1-acid glycoprotein, α-1-antitrypsin, α-2-macroglobulin, apolipoprotein B, C3 complement, C4 complement, haptoglobin, and transferrin). IgA, IgG, and IgM were also part of this profile, but they were analyzed in the immunology assessment (see Chapter 19). Participants who were immunized for

hepatitis B were determined from medical records review and were not considered as positive for serological evidence of prior hepatitis B infection.

All assays for the 2002 gastrointestinal assessment, except for serological evidence of prior hepatitis B infection and antibodies for hepatitis C, were performed by Scripps Clinic. The hepatitis B and C measurements were determined by laboratories at Brooks City-Base. Dade Behring Dimension® RxL equipment was used to quantify AST, ALT, GGT, alkaline phosphatase, total bilirubin, direct bilirubin, LDH, cholesterol, HDL, triglycerides, creatine phosphokinase, serum amylase, and albumin. The Beckman Coulter Immage® System quantified all components of the protein profile except albumin. Prothrombin time was measured on Dade Behring Dimension Blood Coagulation System equipment. Abbott Commander® equipment was used to determine the presence or absence of antibodies for hepatitis A. Serological evidence of prior hepatitis B infection and antibodies for hepatitis C was determined using enzyme Abbott® immunoassays by laboratories at Brooks City-Base. Stool hemoccult was determined using a Beckman Coulter® hemoccult kit.

All laboratory variables were analyzed in both continuous and discrete forms, except for direct bilirubin, antibodies for hepatitis A, serological evidence of prior hepatitis B infection, current hepatitis B, antibodies for hepatitis C, and stool hemoccult, which were analyzed only in discrete form. Direct bilirubin was analyzed only in its discrete form because there were few distinct measurements, precluding a meaningful continuous analysis.

Participants whose blood contained hepatitis B surface antigen or hepatitis C antibodies and participants with body temperatures greater than or equal to 100 degrees Fahrenheit were excluded from the analysis of all laboratory variables, except antibodies for hepatitis A, serological evidence of prior hepatitis B infection, antibodies for hepatitis C, and prothrombin time. For serological evidence of prior hepatitis B infection, participants who had received the hepatitis B vaccine were included in the analysis as negative for serological evidence of prior hepatitis B infection. For the other hepatitis variables, no participants were excluded. Attempts were made to determine, from a medical records review, which occurrences of the types of hepatitis described above were prior to service in SEA, but the date of hepatitis onset was not available for the majority of participants. Consequently, all occurrences of hepatitis were included for these variables. Participants who tested positive for the human immunodeficiency virus (HIV) and participants taking anticoagulants (e.g., Coumadin®) or aspirin were excluded from the prothrombin time analysis.

13.1.3.2 Covariates

Statistical analyses of all medical records variables were adjusted for age, race, military occupation, body mass index, lifetime smoking history, lifetime alcohol history, cumulative industrial chemical exposure, and cumulative degreasing chemical exposure.

Current hepatomegaly was adjusted only for age, race, military occupation, and body mass index. Statistical analyses of all laboratory variables except alkaline phosphatase and α-1-antitrypsin were adjusted for age, race, military occupation, body mass index, current smoking, current alcohol use, lifetime alcohol history, cumulative degreasing chemical exposure, and cumulative industrial chemical exposure.

Age, race, and occupation were determined from military records. Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 2002 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

Body mass index was calculated as weight/(height)^2, where the weight was measured in kilograms and the height was measured in meters at the physical examination (95). For purposes of covariate associations for discrete dependent variables, body fat was dichotomized as "not obese" ($\leq$30 kg/m^2) and "obese" (>30 kg/m^2).

Lifetime alcohol history was based on information from the 2002 questionnaire and combined with similar information gathered at the 1987, 1992, and 1997 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking pattern changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year. Current alcohol use was defined as the average number of drinks per day during the 2 weeks prior to completing the physical examination.

Wine consumption showed a strong inverse association with alkaline phosphatase in the 1985, 1987, 1992, and 1997 follow-up examinations. The inverse association persisted in the 2002 follow-up examination data; therefore, current wine consumption and lifetime wine history replaced current alcohol use and lifetime alcohol history as covariates in the adjusted analyses of alkaline phosphatase. Current wine consumption also replaced current alcohol use in the adjusted analysis of α-1-antitrypsin based on covariate associations in the 1997 follow-up examination data, which showed that α-1-antitrypsin was highly associated with current wine consumption but not associated with current alcohol use.

13.1.4 Statistical Methods

Table 13-1 summarizes the statistical analysis performed for the 2002 gastrointestinal assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, exclusions, and statistical methods. The second part of this table further describes the covariates. A covariate was used in its continuous form whenever possible for adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 13-1.

Table 13-1. Statistical Analysis for the Gastrointestinal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Uncharacterized Hepatitis	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Jaundice (unspecified)	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Chronic Liver Disease and Cirrhosis (alcohol-related)	MR-V	D	Yes No	(1)	(b)	U:LR,CS A:LR

Table 13-1. Statistical Analysis for the Gastrointestinal Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Chronic Liver Disease and Cirrhosis (nonalcohol-related)	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Liver Abscess and Sequelae of Chronic Liver Disease	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Enlarged Liver (hepatomegaly)	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Other Disorders of the Liver	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Current Hepatomegaly	PE	D	Yes No	(2)	(c)	U:LR,CS A:LR
AST (U/L)	LAB	C/D	High: >37 Normal: ≤37	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
ALT (U/L)	LAB	C/D	High: >65 Normal: ≤65	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
GGT (U/L)	LAB	C/D	High: >85 Normal: ≤85	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Alkaline Phosphatase (U/L)	LAB	C/D	High: >136 Normal: ≤136	(4)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Total Bilirubin (mg/dL)	LAB	C/D	High: >1.0 Normal: ≤1.0	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Direct Bilirubin (mg/dL)	LAB	D	High: >0.3 Normal: ≤0.3	(3)	(d)	U:LR,CS A:LR
LDH (U/L)	LAB	C/D	High: >190 Normal: ≤190	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Cholesterol (mg/dL)	LAB	C/D	High: >240 Normal: ≤240	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
HDL Cholesterol (mg/dL)	LAB	C/D	Low: <40 Normal: ≥40	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Cholesterol-HDL Ratio	LAB	C/D	High: >5 Normal: ≤5	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Triglycerides (mg/dL)	LAB	C/D	High: >250 Normal: ≤250	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Creatine Phosphokinase (U/L)	LAB	C/D	High: >232 Normal: ≤232	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Serum Amylase (U/L)	LAB	C/D	High: >115 Normal: ≤115	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Antibodies for Hepatitis A	LAB	D	Yes No	(3)	None	U:LR,CS A:LR
Serological Evidence of Prior Hepatitis B Infection	LAB/ MR-V	D	Yes No	(3)	None	U:LR,CS A:LR
Antibodies for Hepatitis C	LAB	D	Yes No	(3)	None	U:LR,CS A:LR

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Stool Hemoccult	LAB	D	Yes No	(5)	(d)	U:LR,CS A:LR
Protein Profile: Prealbumin (mg/dL)	LAB	C/D	Low: <18 Normal: ≥18	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Protein Profile: Albumin (mg/dL)	LAB	C/D	Low: <3,400 Normal: ≥3,400	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Protein Profile: α-1-Acid Glycoprotein (mg/dL)	LAB	C/D	High: >117 Normal: ≤117	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Protein Profile: α-1-Antitrypsin (mg/dL)	LAB	C/D	Abnormal Low: <88 Normal: 88-174 Abnormal High: >174	(6)	(d)	U:PR,CS,GLM,TT A:PR,GLM
Protein Profile: α-2-Macroglobulin (mg/dL)	LAB	C/D	High: >259 Normal: ≤259	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Protein Profile: Apolipoprotein B (mg/dL)	LAB	C/D	High: >162 Normal: ≤162	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Protein Profile: C3 Complement (mg/dL)	LAB	C/D	Low: <79 Normal: ≥79	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Protein Profile: C4 Complement (mg/dL)	LAB	C/D	Low: <16 Normal: ≥16	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Protein Profile: Haptoglobin (mg/dL)	LAB	C/D	High: >195 Normal: ≤195	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Protein Profile: Transferrin (mg/dL)	LAB	C/D	Low: <202 Normal: ≥202	(3)	(d)	U:LR,CS,GLM,TT A:LR,GLM
Prothrombin Time (seconds)	LAB	C/D	High: >12.3 Normal: ≤12.3	(3)	(e)	U:LR,CS,GLM,TT A:LR,GLM

[a]Covariates:

(1) age, race, military occupation, body mass index, lifetime alcohol history, cumulative industrial chemical exposure, cumulative degreasing chemical exposure, lifetime smoking history.

(2) age, race, military occupation, body mass index.

(3) age, race, military occupation, body mass index, current alcohol consumption, lifetime alcohol history, cumulative industrial chemical exposure, cumulative degreasing chemical exposure, current smoking.

(4) age, race, military occupation, body mass index, current wine consumption, lifetime wine history, cumulative industrial chemical exposure, cumulative degreasing chemical exposure, current smoking.

(5) age, race, military occupation, body mass index, current alcohol consumption, lifetime alcohol history, cumulative industrial chemical exposure, cumulative degreasing chemical exposure, current smoking, compliance to dietary restrictions.

(6) age, race, military occupation, body mass index, current wine consumption, lifetime alcohol history, cumulative industrial chemical exposure, cumulative degreasing chemical exposure, current cigarette smoking.

[b]Exclusions:

(a) participants with a pre-SEA history of the disorder.

(b) participants with a pre-SEA history of the disorder, participants with no lifetime alcohol history.

(c) participants whose blood contained hepatitis B surface antigen or hepatitis C antibodies.

Table 13-1. Statistical Analysis for the Gastrointestinal Assessment (Continued)

(d) participants whose blood contained hepatitis B surface antigen or hepatitis C antibodies, participants with body temperatures greater than or equal to 100 degrees Fahrenheit.

(e) participants testing positive for HIV, participants taking an anticoagulant (e.g., Coumadin®) or aspirin at the time of the examination.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	C/D	Born ≥ 1942 Born < 1942
Race	MIL	D	Black Non-Black
Military Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Cumulative Degreasing Chemical Exposure	Q-SR	D	Yes No
Cumulative Industrial Chemical Exposure	Q-SR	D	Yes No
Body Mass Index (kg/m^2)	PE	C/D	Not Obese: ≤30 Obese: >30
Current Alcohol Use (2 weeks prior to physical exam) (drinks/day)	Q-SR	C/D	0–1 >1
Lifetime Alcohol History (drink-years)	Q-SR	C/D	0 >0–40 >40
Current Cigarette Smoking (cigarettes/day)	Q-SR	C/D	Never Former >0–20 >20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	C/D	0 >0–10 >10
Current Wine Consumption (2 weeks prior to physical exam) (drinks of wine/day)	Q-SR	C/D	0 >0
Lifetime Wine History (drink-years of wine)	Q-SR	C/D	0 >0
Compliance to Dietary Restrictions	PE	D	Yes No

Abbreviations

Data Source: LAB: 2002 laboratory results
MIL: Air Force military records
MR-V: Medical records (verified)
PE: 2002 physical examination
Q-SR: AFHS health questionnaires (self-reported)

Data Form: D: Discrete analysis only

                                    D/C: Discrete and continuous analyses for dependent variables; appropriate form for analysis (either discrete or continuous) for covariates

Statistical Analysis: U: Unadjusted analysis

                                      A: Adjusted analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)

                                    GLM: General linear models analysis

                                    LR: Logistic regression analysis

                                    PR: Polytomous logistic regression analysis

                                    TT: Two-sample t-test

Four models were examined for each dependent variable given in Table 13-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for covariates. These covariates are given in Table 13-1. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. In an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-4, the median level of exposure to dioxin was highest for enlisted groundcrew, followed by enlisted flyers, then officers.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the Centers for Disease Control and Prevention (CDC) using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in parts per trillion (ppt) on a lipid weight basis (96). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2. A statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model to account for body mass index-related differences in elimination rate (97).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. Another category was examined by combining the low and high Ranch Hand categories. This combination is referred to in the tables as the "low plus

high Ranch Hand" category. These five categories—Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the four Ranch Hand categories and the dependent variable in the Comparison category was examined. As in Model 2, a statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables. One Ranch Hand without a dioxin measure was excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The term "unadjusted" was used in the text and tables as follows: Models 1 and 4 did not adjust for any covariates. Models 2 and 3 adjusted only for body mass index at the time of the blood measurement for dioxin. The term "adjusted" was used in the text and tables as follows: Models 1 and 4 adjusted for the covariates shown in Table 13-1 unless otherwise specified by a footnote to the table. Models 2 and 3 additionally adjusted only for body mass index at the time of the blood measurement for dioxin.

Table 13-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants that were excluded from analyses is given.

Table 13-2. Number of Participants Excluded or with Missing Data for the Gastrointestinal Assessment

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Current Hepatomegaly	DEP	1	0	0	1	1	0
Antibodies for Hepatitis A	DEP	3	1	1	3	3	1
Stool Hemoccult	DEP	47	77	25	47	47	77
Prothrombin Time	DEP	1	0	0	1	1	0
Body Mass Index	COV	1	0	0	1	1	0
Current Alcohol Use	COV	0	2	0	0	0	2
Current Wine Use	COV	0	2	0	0	0	2
Lifetime Alcohol History	COV	4	5	3	4	4	5
Lifetime Wine History	COV	1	4	1	1	1	4
Current Cigarette Smoking	COV	0	2	0	0	0	2
Lifetime Cigarette Smoking History	COV	0	3	0	0	0	3
Pre-SEA Uncharacterized Hepatitis	EXC	6	6	3	6	6	6
Pre-SEA Jaundice	EXC	21	28	9	21	21	28
Chronic Liver Disease and Cirrhosis (alcohol-related)	EXC	1	3	1	1	1	3
Enlarged Liver (hepatomegaly)	EXC	1	1	1	1	1	1
Other Disorders of the Liver	EXC	3	9	0	3	3	9
No Lifetime Alcohol History	EXC	48	59	29	48	48	59
Hepatitis B Surface Antigen	EXC	1	0	1	1	1	0

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Body Temperature $\geq$ 100 °F at the Time of the 2002 Physical Examination	EXC	3	1	2	3	3	1
HIV Positive	EXC	3	2	3	3	3	2
Participants Taking an Anticoagulant or Aspirin at the Time of the 2002 Physical Examination	EXC	203	278	120	203	203	278

[a]777 Ranch Hands and 1,174 Comparisons for group.
[b]424 Ranch Hands for initial dioxin; 776 Ranch Hands for 1987 dioxin.
[c]776 Ranch Hands and 1,174 Comparisons for categorized dioxin.

Note: DEP = Dependent variable.
      COV = Covariate.
      EXC = Exclusion.

13.2   RESULTS

13.2.1   Dependent Variable-covariate Associations

The gastrointestinal dependent variables were tested for associations with each of the covariates used in the adjusted analyses. The complete results are presented in Appendix F, Table F-5. These associations were pairwise between the dependent variable and the covariate and were not adjusted for any other covariates. A brief summary of the pattern of significant ($p \leq 0.05$) dependent variable-covariate associations is described in the following paragraphs. In the discussion of the results below, low levels are considered adverse for HDL cholesterol, prealbumin, albumin, C3 complement, C4 complement, and transferrin.

13.2.1.1 Age

Total bilirubin, LDH, HDL cholesterol, serum amylase, α-1-antitrypsin, α-2-macroglobulin, haptoglobin, and prothrombin time increased with age. ALT, GGT, alkaline phosphatase, cholesterol, cholesterol-HDL ratio, triglycerides, creatine phosphokinase, prealbumin, albumin, apolipoprotein B, C3 complement, C4 complement, and transferrin decreased with increasing age.

Older participants had more abnormal levels of LDH, α-2-macroglobulin, C3 complement, transferrin, and prothrombin time and were more likely to have hepatitis A than younger participants. Younger participants, however, were more likely to have had abnormal levels of ALT, GGT, alkaline phosphatase, cholesterol, cholesterol-HDL ratio, and triglycerides than older participants.

13.2.1.2 Race

Black participants had higher mean GGT, creatine phosphokinase, and serum amylase levels and lower mean albumin and transferrin levels than did non-Black participants. Non-Black participants had higher mean total bilirubin, triglycerides, and α-2-macroglobulin levels and had lower mean HDL cholesterol, C3 complement, and C4 complement levels than Black participants.

Black participants had a greater percentage of abnormal creatine phosphokinase, serum amylase, and albumin values and had more occurrences of other liver disorders, antibodies for hepatitis A, prior hepatitis B infections, and antibodies for hepatitis C than did non-Black participants. Non-Black participants had a higher percentage of abnormal HDL cholesterol, cholesterol-HDL ratio, and α-2-macroglobulin values.

13.2.1.3 Military Occupation

Enlisted groundcrew had higher mean ALT, GGT, alkaline phosphatase, cholesterol, cholesterol-HDL ratio, triglycerides, creatine phosphokinase, α-1-acid glycoprotein and apolipoprotein B levels, and lower mean HDL levels than officers or enlisted flyers. Mean levels of α-1-antitrypsin, α-2-macroglobulin, and haptoglobin were higher for enlisted flyers than for officers or enlisted groundcrew. Officers had higher mean total bilirubin levels and lower C3 complement, C4 complement, and transferrin levels than enlisted personnel.

Enlisted groundcrew were more likely to have abnormal cholesterol, HDL cholesterol, cholesterol-HDL ratio, and triglyceride values, and were more likely to have antibodies to hepatitis C than officers or enlisted flyers. Enlisted flyers had more abnormal alkaline phosphatase, α-1-antitrypsin, and haptoglobin levels than enlisted groundcrew, and they were more likely to have antibodies to hepatitis A or a prior hepatitis B infection than enlisted groundcrew or officers. Officers had a higher percentage of abnormal C3 complement levels than enlisted personnel.

13.2.1.4 Cumulative Degreasing Chemical Exposure

Participants exposed to degreasing chemicals had higher mean levels of the following: alkaline phosphatase, cholesterol-HDL ratio, triglycerides, α-1-acid glycoprotein, α-1-antitrypsin, apolipoprotein B, and haptoglobin. Mean total bilirubin levels were higher and C3 complement, C4 complement, and transferrin levels were lower in participants not exposed to degreasing chemicals. Mean HDL levels were lower in participants with degreasing chemical exposure.

More abnormalities in cholesterol, HDL cholesterol, cholesterol-HDL ratio, triglycerides, α-1-antitrypsin, and haptoglobin were seen in participants exposed to degreasing chemicals, and more abnormal C3 complement levels were seen in participants who were not exposed.

13.2.1.5 Cumulative Industrial Chemical Exposure

Higher mean levels of cholesterol, cholesterol-HDL ratio, triglycerides, α-1-antitrypsin, and apolipoprotein B, and lower mean levels of HDL cholesterol were seen in participants exposed to industrial chemicals. Mean levels of AST, total bilirubin, and prothrombin time were higher and mean C3 complement and C4 complement levels were lower in participants not exposed to industrial chemicals than in participants with exposure.

Significantly more abnormal cholesterol, HDL cholesterol, cholesterol-HDL ratio, triglycerides, and α-1-antitrypsin levels were seen in participants with industrial chemical exposure, as was a higher prevalence of chronic alcohol-related liver disease and cirrhosis.

13.2.1.6 Body Mass Index

AST, ALT, GGT, LDH, cholesterol-HDL ratio, triglycerides, creatine phosphokinase, C3 complement, C4 complement, haptoglobin, and transferrin increased with body mass index. Cholesterol, HDL cholesterol, amylase, prealbumin, albumin, and α-1-antitrypsin decreased with increasing body mass index.

The percent of abnormal values for amylase, α-1-antitrypsin, and C3 complement, and the prevalence of hepatitis C antibodies was higher in participants who were not obese than in obese participants. Obese participants, however, had more abnormal levels of ALT, LDH, HDL cholesterol, cholesterol-HDL ratio, triglycerides, creatine phosphokinase, and α-2-macroglobulin. Obese participants also were more likely to have chronic liver disease and cirrhosis (nonalcohol-related), other disorders of the liver, and current hepatomegaly than participants who were not obese.

13.2.1.7 Current Alcohol Use

As current alcohol increased, AST, ALT, GGT, total bilirubin, cholesterol, HDL cholesterol, prealbumin, and α-1-acid glycoprotein increased, but the cholesterol-HDL ratio, creatine phosphokinase, amylase, α-2-macroglobulin, and C3 complement levels decreased.

Abnormal levels of HDL cholesterol, cholesterol-HDL ratio, and α-2-macroglobulin were more prevalent in participants consuming no more than one drink per day (in the past 2 weeks) than in participants consuming more than one drink per day. AST, GGT, total bilirubin, and direct bilirubin levels were more likely to be abnormal in participants consuming more than one drink per day over the last 2 weeks.

13.2.1.8 Lifetime Alcohol History

AST, GGT, cholesterol, HDL cholesterol, prealbumin, α-1-acid glycoprotein, α-1-antitrypsin, and haptoglobin levels increased with increasing lifetime alcohol consumption. Cholesterol-HDL ratio and creatine phosphokinase, however, decreased with increasing lifetime alcohol consumption.

Nondrinkers had more abnormal levels of HDL cholesterol, cholesterol-HDL ratio, and α-2-macroglobulin and were more likely to have had uncharacterized hepatitis and hepatitis A antibodies than moderate or heavy drinkers. The heaviest drinkers (>40 drink-years) were more likely to have abnormal GGT, direct bilirubin, α-1-acid glycoprotein, and α-1-antitrypsin levels than moderate drinkers or nondrinkers. Heavy drinkers also were more likely to have chronic liver disease and cirrhosis (alcohol-related), enlarged liver, prior hepatitis B infection, and hepatitis C antibodies than moderate or nondrinkers.

13.2.1.9 Current Cigarette Smoking

As current cigarette smoking increased, GGT, alkaline phosphatase, cholesterol-HDL ratio, α-1-acid glycoprotein, α-1-antitrypsin, and haptoglobin levels increased. AST, ALT, total bilirubin, LDH, creatine phosphokinase, prealbumin, albumin, and prothrombin time decreased with increased current cigarette smoking.

Former cigarette smokers had more abnormal levels of LDH and creatine phosphokinase than nonsmokers or current smokers. Moderate smokers (up to 20 cigarettes per day) were more likely to have hepatitis C antibodies and abnormal levels of alkaline phosphatase and direct bilirubin than heavy smokers, former, or nonsmokers. The heaviest cigarette smokers were more likely to have abnormal cholesterol-HDL ratio, α-1-acid glycoprotein, α-1-antitrypsin, and haptoglobin levels and were more likely to have had a prior hepatitis B infection.

13.2.1.10 Lifetime Cigarette Smoking History

Lifetime cigarette smoking was not significantly associated with any of the dependent variables.

13.2.1.11 Current Wine Consumption

As current wine consumption increased, alkaline phosphatase and α-1-antitrypsin levels decreased. Nonwine drinkers were more likely to have had abnormal alkaline phosphatase and α-1-antitrypsin levels than current wine drinkers.

13.2.1.12 Lifetime Wine History

As lifetime wine consumption increased, alkaline phosphatase levels decreased.

13.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 13-1. Dependent variables are grouped into three sections: (1) gastrointestinal variables derived from the questionnaire that was administered at the 2002 follow-up and previous AFHS examinations and subsequently verified from a review of participant medical records, (2) hepatomegaly, as determined at the 2002 physical examination, and (3) gastrointestinal laboratory variables.

13.2.2.1 Medical Records Variables

13.2.2.1.1 Uncharacterized Hepatitis

All Model 1, 2, and 4 unadjusted and adjusted analyses of uncharacterized hepatitis were nonsignificant (Table 13-3(a-d,g,h): $p > 0.21$ for each analysis).

The unadjusted Model 3 analysis revealed a significant difference in occurrences of uncharacterized hepatitis between Ranch Hands in the high dioxin category and Comparisons (Table 13-3(e): Unadjusted Relative Risk [RR]=2.54, p=0.045). After adjusting for covariates, however, the results became nonsignificant (Table 13-3(f): p=0.083). All other unadjusted and adjusted Model 3 contrasts were nonsignificant (Table 13-3(e,f): $p > 0.23$ for each contrast).

Table 13-3. Analysis of Uncharacterized Hepatitis

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*15 (1.9)*	*1.53 (0.74,3.14)*	*0.253*
	Comparison	*1,168*	*15 (1.3)*		
Officer	Ranch Hand	305	3 (1.0)	0.75 (0.19,3.01)	0.681
	Comparison	457	6 (1.3)		
Enlisted Flyer	Ranch Hand	133	3 (2.3)	4.25 (0.44,41.28)	0.213
	Comparison	185	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	333	9 (2.7)	1.80 (0.69,4.71)	0.232
	Comparison	526	8 (1.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,928*	*1.53 (0.74,3.15)*	*0.255*
Officer	761	0.75 (0.19,3.04)	0.688
Enlisted Flyer	315	3.72 (0.38,36.41)	0.259
Enlisted Groundcrew	852	1.82 (0.69,4.80)	0.224

(c) MODEL 2: RANCH HANDS − INITIAL DIOXIN − UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	1 (0.7)	1.21 (0.78,1.89)	0.410
Medium	142	5 (3.5)		
High	140	4 (2.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS − INITIAL DIOXIN − ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	1.10 (0.64,1.89)	0.738

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, cumulative degreasing chemical exposure, and cumulative industrial chemical exposure because of the sparse number of Ranch Hands with uncharacterized hepatitis.

Table 13-3. *Analysis of Uncharacterized Hepatitis (Continued)*

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,168	15 (1.3)		
Background RH	349	5 (1.4)	1.17 (0.42,3.25)	0.769
Low RH	210	3 (1.4)	1.10 (0.32,3.83)	0.883
High RH	211	7 (3.3)	2.54 (1.02,6.35)	0.045*
Low plus High RH	421	10 (2.4)	1.67 (0.71,3.93)	0.238

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,162		
Background RH	347	1.26 (0.44,3.62)	0.671
Low RH	209	1.18 (0.33,4.19)	0.796
High RH	209	2.36 (0.89,6.24)	0.083
Low plus High RH	418	1.67 (0.70,3.99)	0.249

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	4 (1.5)	1.07 (0.78,1.46)	0.679
Medium	255	3 (1.2)		
High	256	8 (3.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 13-3. Analysis of Uncharacterized Hepatitis (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
765	1.02 (0.71,1.45)	0.931

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.1.2   Unspecified Jaundice

The unadjusted and adjusted Model 1 and 2 analyses of jaundice revealed no significant results (Table 13-4(a-d): p≥0.15 for each analysis).

A significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons was seen in each of the unadjusted and adjusted Model 3 analyses (Table 13-4(e,f): Unadjusted RR=0.24, p=0.024; Adjusted RR=0.24, p=0.027). Ranch Hands in the low and high dioxin categories combined had fewer occurrences of unspecified jaundice than Comparisons (0.7% versus 2.9%, respectively). Each of the remaining contrasts in the unadjusted and adjusted Model 3 analyses were nonsignificant (Table 13-4(e,f): p>0.07 for each contrast).

Both the unadjusted and adjusted Model 4 analyses revealed a significant inverse association between 1987 dioxin and unspecified jaundice (Table 13-4(g,h): Unadjusted RR=0.60, p=0.004; Adjusted RR=0.59, p=0.014). The percentages of Ranch Hands with jaundice in the low, medium, and high 1987 dioxin categories were 3.2, 2.0, and 0.4, respectively.

Table 13-4. Analysis of Unspecified Jaundice

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*756*	*14 (1.9)*	*0.64 (0.34,1.20)*	*0.150*
	Comparison	*1,146*	*33 (2.9)*		
Officer	Ranch Hand	297	7 (2.4)	0.65 (0.27,1.61)	0.354
	Comparison	449	16 (3.6)		
Enlisted Flyer	Ranch Hand	131	2 (1.5)	2.76 (0.25,30.76)	0.409
	Comparison	179	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	328	5 (1.5)	0.49 (0.18,1.34)	0.163
	Comparison	518	16 (3.1)		

Table 13-4. Analysis of Unspecified Jaundice (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,892*	*0.64 (0.34,1.20)*	*0.153*
Officer	745	0.66 (0.27,1.63)	0.368
Enlisted Flyer	307	2.50 (0.22,28.01)	0.457
Enlisted Groundcrew	840	0.48 (0.17,1.32)	0.155

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	137	2 (1.5)	0.74 (0.27,2.05)	0.545
Medium	141	0 (0.0)		
High	137	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
413	0.97 (0.33,2.86)	0.951

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with unspecified jaundice.

Table 13-4. Analysis of Unspecified Jaundice (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,146	33 (2.9)		
Background RH	340	11 (3.2)	1.09 (0.54,2.20)	0.803
Low RH	207	2 (1.0)	0.33 (0.08,1.39)	0.131
High RH	208	1 (0.5)	0.17 (0.02,1.23)	0.079
Low plus High RH	415	3 (0.7)	0.24 (0.07,0.82)	0.024*

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,140		
Background RH	338	1.06 (0.52,2.17)	0.867
Low RH	206	0.33 (0.08,1.40)	0.133
High RH	207	0.18 (0.02,1.31)	0.090
Low plus High RH	413	0.24 (0.07,0.85)	0.027*

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-4. Analysis of Unspecified Jaundice (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
Low	252	8 (3.2)	0.60 (0.42,0.85)	0.004**
Medium	250	5 (2.0)		
High	253	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value$\leq$0.010).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
751	0.59 (0.39,0.90)	0.014*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value$\leq$0.050).

13.2.2.1.3   *Chronic Liver Disease and Cirrhosis (Alcohol-related)*

No significant differences between Ranch Hands and Comparisons were revealed in the unadjusted and adjusted Model 1 analyses of alcohol-related chronic liver disease and cirrhosis (Table 13-5(a,b): p>0.23 for each analysis).

A significant positive relation between initial dioxin and alcohol-related chronic liver disease and cirrhosis was revealed in the unadjusted Model 2 analysis (Table 13-5(c): Unadjusted RR=1.46, p=0.029). After adjusting for covariates, the results became nonsignificant (Table 13-5(d): p=0.272).

All unadjusted and adjusted Model 3 and 4 results were nonsignificant (Table 13-5(e-h): p>0.09 for each analysis).

Table 13-5. Analysis of Chronic Liver Disease and Cirrhosis (Alcohol-related)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*728*	*33 (4.5)*	*1.13 (0.71,1.78)*	*0.614*
	Comparison	*1,112*	*45 (4.0)*		
Officer	Ranch Hand	296	12 (4.1)	1.65 (0.72,3.79)	0.237
	Comparison	441	11 (2.5)		
Enlisted Flyer	Ranch Hand	120	5 (4.2)	1.25 (0.37,4.18)	0.721
	Comparison	178	6 (3.4)		
Enlisted Groundcrew	Ranch Hand	312	16 (5.1)	0.90 (0.48,1.69)	0.738
	Comparison	493	28 (5.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,829*	*1.10 (0.68,1.79)*	*0.690*
Officer	736	1.59 (0.68,3.71)	0.281
Enlisted Flyer	295	1.25 (0.36,4.34)	0.720
Enlisted Groundcrew	798	0.84 (0.43,1.67)	0.626

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	133	2 (1.5)	1.46 (1.05,2.03)	0.029*
Medium	136	5 (3.7)		
High	125	10 (8.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
391	1.28 (0.83,1.97)	0.272

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,112	45 (4.0)		
Background RH	333	16 (4.8)	1.24 (0.69,2.22)	0.481
Low RH	201	5 (2.5)	0.60 (0.23,1.52)	0.280
High RH	193	12 (6.2)	1.52 (0.79,2.95)	0.211
Low plus High RH	394	17 (4.3)	0.94 (0.51,1.75)	0.855

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,106		
Background RH	331	1.37 (0.73,2.58)	0.322
Low RH	200	0.66 (0.25,1.72)	0.395
High RH	191	1.16 (0.56,2.44)	0.686
Low plus High RH	391	0.87 (0.46,1.66)	0.673

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	247	10 (4.0)	1.20 (0.97,1.48)	0.098
Medium	242	9 (3.7)		
High	238	14 (5.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log$_2$ (1987 Dioxin)		
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
722	1.08 (0.83,1.41)	0.577

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.1.4   Chronic Liver Disease and Cirrhosis (Nonalcohol-related)

All unadjusted and adjusted Model 1 through 4 analyses of nonalcohol-related chronic liver disease and cirrhosis were nonsignificant (Table 13-6(a-h): p>0.06 for each analysis).

Table 13-6. Analysis of Chronic Liver Disease and Cirrhosis (Nonalcohol-related)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Yes**	**Unadjusted Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*777*	*27 (3.5)*	*1.53 (0.89,2.63)*	*0.125*
	Comparison	*1,174*	*27 (2.3)*		
Officer	Ranch Hand	307	11 (3.6)	2.11 (0.84,5.30)	0.113
	Comparison	462	8 (1.7)		
Enlisted Flyer	Ranch Hand	133	1 (0.8)	0.19 (0.02,1.58)	0.126
	Comparison	185	7 (3.8)		
Enlisted Groundcrew	Ranch Hand	337	15 (4.5)	2.00 (0.92,4.33)	0.079
	Comparison	527	12 (2.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED			
Occupational Category	**n**	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	*1,940*	*1.50 (0.87,2.60)*	*0.144*
Officer	768	2.07 (0.82,5.23)	0.124
Enlisted Flyer	315	0.18 (0.02,1.50)	0.113
Enlisted Groundcrew	857	1.98 (0.91,4.31)	0.086

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a,b]**	**p-Value**
Low	140	5 (3.6)	1.00 (0.71,1.40)	0.979
Medium	143	9 (6.3)		
High	141	5 (3.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
421	1.22 (0.78,1.90)	0.377

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	27 (2.3)		
Background RH	352	8 (2.3)	1.17 (0.52,2.62)	0.705
Low RH	211	9 (4.3)	1.76 (0.81,3.83)	0.156
High RH	213	10 (4.7)	1.80 (0.85,3.83)	0.124
Low plus High RH	424	19 (4.5)	1.78 (0.97,3.27)	0.063

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	350	1.21 (0.53,2.76)	0.653
Low RH	210	1.76 (0.79,3.89)	0.164
High RH	211	1.77 (0.81,3.89)	0.155
Low plus High RH	421	1.76 (0.95,3.27)	0.071

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	7 (2.7)	1.15 (0.91,1.45)	0.244
Medium	258	7 (2.7)		
High	258	13 (5.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
771	1.02 (0.76,1.38)	0.883

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.1.5   Liver Abscess and Sequelae of Chronic Liver Disease

No significant associations with group or dioxin were seen in the analysis of liver abscess and sequelae of chronic liver disease in each of the unadjusted and adjusted Model 1 through 4 analyses (Table 13-7(a-h): p>0.06 for each analysis).

Table 13-7. Analysis of Liver Abscess and Sequelae of Chronic Liver Disease

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*5 (0.6)*	*3.80 (0.73,19.61)*	*0.090*
	Comparison	*1,174*	*2 (0.2)*		
Officer	Ranch Hand	307	2 (0.7)	3.02 (0.27,33.48)	0.367
	Comparison	462	1 (0.2)		
Enlisted Flyer	Ranch Hand	133	0 (0.0)	--	--
	Comparison	185	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	337	3 (0.9)	4.72 (0.49,45.61)	0.180
	Comparison	527	1 (0.2)		

--: Results were not presented because of the sparse number of participants with a history of liver abscess or sequelae of chronic liver disease.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,940*	*3.97 (0.76,20.87)*	*0.082*
Officer	768	3.05 (0.27,33.85)	0.364
Enlisted Flyer	315	--	--
Enlisted Groundcrew	857	5.03 (0.50,50.97)	0.172

--: Results were not presented because of the sparse number of participants with a history of liver abscess or sequelae of chronic liver disease.

Note: Results were not adjusted for race and military occupation because of the sparse number of participants with a history of liver abscess or sequelae of chronic liver disease.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	1 (0.7)	1.28 (0.58,2.82)	0.557
Medium	143	1 (0.7)		
High	141	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-7. Analysis of Liver Abscess and Sequelae of Chronic Liver Disease (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
421	1.63 (0.67,3.96)	0.297

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with a history of liver abscess or sequelae of chronic liver disease.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	2 (0.2)		
Background RH	352	2 (0.6)	3.18 (0.44,22.96)	0.251
Low RH	211	1 (0.5)	2.83 (0.25,31.33)	0.397
High RH	213	2 (0.9)	5.81 (0.81,41.95)	0.081
Low plus High RH	424	3 (0.7)	4.06 (0.64,25.57)	0.136

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	350	3.05 (0.42,22.37)	0.273
Low RH	210	3.01 (0.26,34.33)	0.376
High RH	211	7.06 (0.90,55.13)	0.062
Low plus High RH	421	4.61 (0.70,30.20)	0.111

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

       Results were not adjusted for race and military occupation because of the sparse number of participants with a history of liver abscess or sequelae of chronic liver disease.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	1 (0.4)	1.05 (0.61,1.80)	0.860
Medium	258	2 (0.8)		
High	258	2 (0.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
771	1.14 (0.63,2.06)	0.679

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with a history of liver abscess or sequelae of chronic liver disease.

13.2.2.1.6   Enlarged Liver (Hepatomegaly)

All unadjusted and adjusted Model 1 through 4 analyses of enlarged liver were nonsignificant (Table 13-8(a-h): p>0.28 for each analysis).

Table 13-8. Analysis of Enlarged Liver (Hepatomegaly)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*776*	*27 (3.5)*	*0.90 (0.56,1.47)*	*0.682*
	Comparison	*1,173*	*45 (3.8)*		
Officer	Ranch Hand	307	11 (3.6)	1.19 (0.53,2.65)	0.676
	Comparison	461	14 (3.0)		
Enlisted Flyer	Ranch Hand	133	5 (3.8)	1.17 (0.35,3.90)	0.804
	Comparison	185	6 (3.2)		
Enlisted Groundcrew	Ranch Hand	336	11 (3.3)	0.68 (0.33,1.40)	0.295
	Comparison	527	25 (4.7)		

Table 13-8. Analysis of Enlarged Liver (Hepatomegaly) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,938*	*0.92 (0.56,1.51)*	*0.746*
Officer	767	1.20 (0.54,2.70)	0.654
Enlisted Flyer	315	1.17 (0.35,3.97)	0.798
Enlisted Groundcrew	856	0.69 (0.33,1.44)	0.324

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	4 (2.9)	0.87 (0.58,1.30)	0.474
Medium	143	8 (5.6)		
High	140	3 (2.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
420	0.78 (0.49,1.25)	0.286

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with a history of enlarged liver.

Table 13-8. Analysis of Enlarged Liver (Hepatomegaly) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,173	45 (3.8)		
Background RH	352	12 (3.4)	0.95 (0.49,1.82)	0.872
Low RH	211	7 (3.3)	0.84 (0.37,1.89)	0.671
High RH	212	8 (3.8)	0.93 (0.43,2.00)	0.844
Low plus High RH	423	15 (3.5)	0.88 (0.48,1.60)	0.678

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,167		
Background RH	350	1.03 (0.53,2.00)	0.938
Low RH	210	0.87 (0.38,1.99)	0.748
High RH	210	0.87 (0.39,1.94)	0.735
Low plus High RH	420	0.87 (0.47,1.61)	0.661

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	10 (3.8)	0.93 (0.73,1.19)	0.572
Medium	258	7 (2.7)		
High	257	10 (3.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 13-8. Analysis of Enlarged Liver (Hepatomegaly) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
770	0.91 (0.69,1.21)	0.513

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.1.7 Other Disorders of the Liver

No significant relations with group or dioxin were revealed in the unadjusted or adjusted Model 1 through 4 analyses of other disorders of the liver (Table 13-9(a-h): $p \geq 0.24$ for each analysis).

Table 13-9. Analysis of Other Disorders of the Liver

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*774*	*365 (47.2)*	*1.08 (0.90,1.30)*	*0.406*
	Comparison	*1,165*	*527 (45.2)*		
Officer	Ranch Hand	305	134 (43.9)	1.01 (0.76,1.36)	0.936
	Comparison	456	199 (43.6)		
Enlisted Flyer	Ranch Hand	133	68 (51.1)	1.15 (0.74,1.80)	0.531
	Comparison	185	88 (47.6)		
Enlisted Groundcrew	Ranch Hand	336	163 (48.5)	1.11 (0.85,1.47)	0.437
	Comparison	524	240 (45.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,928*	*1.08 (0.89,1.30)*	*0.442*
Officer	760	1.01 (0.75,1.36)	0.941
Enlisted Flyer	315	1.14 (0.72,1.80)	0.566
Enlisted Groundcrew	853	1.11 (0.84,1.47)	0.461

Table 13-9. Analysis of Other Disorders of the Liver (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Yes**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	140	65 (46.4)	1.01 (0.87,1.17)	0.902
Medium	143	75 (52.4)		
High	141	70 (49.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
421	1.04 (0.87,1.23)	0.687

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,165	527 (45.2)		
Background RH	349	155 (44.4)	1.04 (0.81,1.33)	0.761
Low RH	211	103 (48.8)	1.14 (0.84,1.53)	0.400
High RH	213	107 (50.2)	1.15 (0.86,1.55)	0.345
Low plus High RH	424	210 (49.5)	1.14 (0.91,1.43)	0.240

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-9. Analysis of Other Disorders of the Liver (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,159		
Background RH	347	1.06 (0.82,1.36)	0.660
Low RH	210	1.08 (0.80,1.46)	0.612
High RH	211	1.16 (0.85,1.58)	0.355
Low plus High RH	421	1.12 (0.89,1.41)	0.341

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	258	116 (45.0)	1.04 (0.95,1.14)	0.354
Medium	257	120 (46.7)		
High	258	129 (50.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	1.02 (0.91,1.13)	0.756

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.2 Physical Examination Variable

13.2.2.2.1   Current Hepatomegaly

All unadjusted and adjusted Model 1 through 4 analyses of current hepatomegaly were nonsignificant (Table 13-10(a-h): p>0.17 for each analysis).

Table 13-10. Analysis of Current Hepatomegaly

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*12 (1.6)*	*1.39 (0.63,3.06)*	*0.415*
	Comparison	*1,155*	*13 (1.1)*		
Officer	Ranch Hand	305	6 (2.0)	2.29 (0.64,8.17)	0.203
	Comparison	460	4 (0.9)		
Enlisted Flyer	Ranch Hand	133	0 (0.0)	--	0.224[a]
	Comparison	181	4 (2.2)		
Enlisted Groundcrew	Ranch Hand	332	6 (1.8)	1.87 (0.57,6.19)	0.303
	Comparison	514	5 (1.0)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with current hepatomegaly.

--: Results were not presented because of the sparse number of participants with current hepatomegaly.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,925*	*1.37 (0.62,3.02)*	*0.440*
Officer	765	2.25 (0.63,8.04)	0.214
Enlisted Flyer	314	--	--
Enlisted Groundcrew	846	1.83 (0.55,6.06)	0.323

--: Results were not presented because of the sparse number of participants with current hepatomegaly.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	3 (2.2)	0.79 (0.43,1.47)	0.438
Medium	141	2 (1.4)		
High	141	2 (1.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-10. Analysis of Current Hepatomegaly (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
421	0.73 (0.38,1.42)	0.337

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with current hepatomegaly.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,155	13 (1.1)		
Background RH	348	5 (1.4)	1.42 (0.50,4.06)	0.508
Low RH	209	5 (2.4)	2.06 (0.72,5.87)	0.175
High RH	212	2 (0.9)	0.76 (0.17,3.41)	0.720
Low plus High RH	421	7 (1.7)	1.25 (0.46,3.38)	0.664

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155		
Background RH	348	1.46 (0.50,4.27)	0.486
Low RH	209	2.03 (0.70,5.88)	0.189
High RH	212	0.70 (0.15,3.23)	0.643
Low plus High RH	421	1.19 (0.43,3.25)	0.741

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-10. Analysis of Current Hepatomegaly (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	5 (2.0)	0.98 (0.69,1.40)	0.913
Medium	257	4 (1.6)		
High	256	3 (1.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
769	0.94 (0.64,1.36)	0.733

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with current hepatomegaly.

13.2.2.3 Laboratory Variables

13.2.2.3.1   AST (Continuous)

No significant relations were revealed in the unadjusted and adjusted Model 1 through 4 analyses of AST in its continuous form (Table 13-11(a-h): p>0.05 for each analysis).

Table 13-11. Analysis of AST (U/L) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*24.49*	*0.32*	*0.363*
	Comparison	*1,154*	*24.17*		
Officer	Ranch Hand	305	25.37	1.03	0.075
	Comparison	459	24.34		
Enlisted Flyer	Ranch Hand	133	23.15	-0.70	0.406
	Comparison	181	23.85		
Enlisted Groundcrew	Ranch Hand	330	24.26	0.13	0.812
	Comparison	514	24.13		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*24.78*	*0.42*	*0.237*
	Comparison	*1,149*	*24.36*		
Officer	Ranch Hand	304	25.72	1.12	0.053
	Comparison	459	24.60		
Enlisted Flyer	Ranch Hand	132	23.82	-0.48	0.574
	Comparison	179	24.30		
Enlisted Groundcrew	Ranch Hand	327	24.51	0.15	0.785
	Comparison	511	24.36		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 13-11. Analysis of AST (U/L) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	24.90	24.93	0.003	-0.009 (0.012)	0.451
Medium	141	24.33	24.34			
High	140	24.38	24.34			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of AST versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	24.39	0.095	0.000 (0.014)	0.990
Medium	140	24.38			
High	138	24.42			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of AST versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	24.17	24.17		
Background RH	348	24.44	24.43	0.26	0.578
Low RH	208	24.86	24.86	0.69	0.235
High RH	211	24.22	24.22	0.05	0.930
Low plus High RH	419	24.53	24.54	0.37	0.404

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-11. Analysis of AST (U/L) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	24.39		
Background RH	346	24.65	0.26	0.582
Low RH	207	25.11	0.72	0.217
High RH	209	24.58	0.19	0.740
Low plus High RH	416	24.84	0.45	0.305

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	24.19	<0.001	-0.000 (0.008)	0.977
Medium	256	25.09			
High	255	24.19			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of AST versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	23.90	0.055	0.004 (0.009)	0.645
Medium	255	25.03			
High	252	24.32			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of AST versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.2   AST (Discrete)

Each of the unadjusted and adjusted Model 1 through 4 analyses of AST in its discrete form was nonsignificant (Table 13-12(a-h): $p \geq 0.12$ for each analysis).

Table 13-12. Analysis of AST (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*65 (8.5)*	*1.19 (0.85,1.67)*	*0.308*
	Comparison	*1,154*	*83 (7.2)*		
Officer	Ranch Hand	305	29 (9.5)	1.50 (0.88,2.56)	0.134
	Comparison	459	30 (6.5)		
Enlisted Flyer	Ranch Hand	133	10 (7.5)	1.26 (0.52,3.05)	0.614
	Comparison	181	11 (6.1)		
Enlisted Groundcrew	Ranch Hand	330	26 (7.9)	0.96 (0.58,1.60)	0.879
	Comparison	514	42 (8.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*1.22 (0.87,1.72)*	*0.253*
Officer	763	1.53 (0.90,2.62)	0.120
Enlisted Flyer	311	1.36 (0.55,3.33)	0.503
Enlisted Groundcrew	838	0.96 (0.57,1.61)	0.884

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	9 (6.5)	1.09 (0.85,1.41)	0.508
Medium	141	12 (8.5)		
High	140	13 (9.3)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-12. Analysis of AST (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
416	1.24 (0.87,1.77)	0.229

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	83 (7.2)		
Background RH	348	31 (8.9)	1.30 (0.84,2.01)	0.234
Low RH	208	17 (8.2)	1.14 (0.66,1.96)	0.643
High RH	211	17 (8.1)	1.10 (0.64,1.90)	0.732
Low plus High RH	419	34 (8.1)	1.12 (0.74,1.70)	0.599

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	1.38 (0.88,2.15)	0.163
Low RH	207	1.19 (0.68,2.08)	0.535
High RH	209	1.02 (0.57,1.80)	0.952
Low plus High RH	416	1.10 (0.72,1.69)	0.659

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-12. Analysis of AST (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) High**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	256	21 (8.2)	1.04 (0.89,1.22)	0.596
Medium	256	22 (8.6)		
High	255	22 (8.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
762	1.06 (0.87,1.29)	0.574

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.3   ALT (Continuous)

All unadjusted and adjusted Model 1 through 4 analyses of ALT in its continuous form were
nonsignificant (Table 13-13(a-h): p>0.05 for each analysis).

Table 13-13. Analysis of ALT (U/L) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*44.76*	*0.16*	*0.772*
	Comparison	*1,154*	*44.60*		
Officer	Ranch Hand	305	44.83	1.18	0.180
	Comparison	459	43.65		
Enlisted Flyer	Ranch Hand	133	43.00	-0.66	0.620
	Comparison	181	43.66		
Enlisted Groundcrew	Ranch Hand	330	45.42	-0.38	0.663
	Comparison	514	45.80		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented
  because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 13-13. Analysis of ALT (U/L) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*44.45*	*0.38*	*0.480*
	Comparison	*1,149*	*44.07*		
Officer	Ranch Hand	304	45.59	1.45	0.088
	Comparison	459	44.14		
Enlisted Flyer	Ranch Hand	132	44.06	-0.04	0.977
	Comparison	179	44.10		
Enlisted Groundcrew	Ranch Hand	327	43.56	-0.44	0.578
	Comparison	511	44.00		

[a]Transformed from natural logarithm scale.

[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	44.60	44.65	0.006	0.008 (0.010)	0.398
Medium	141	45.76	45.78			
High	140	46.24	46.16			

[a]Transformed from natural logarithm scale.

[b]Adjusted for body mass index at the time of the blood measurement of dioxin.

[c]Slope and standard error based on natural logarithm of ALT versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	45.24	0.153	0.009 (0.011)	0.390
Medium	140	46.31			
High	138	46.73			

[a]Transformed from natural logarithm scale.

[b]Slope and standard error based on natural logarithm of ALT versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-13. Analysis of ALT (U/L) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	44.60	44.59		
Background RH	348	43.90	44.01	-0.58	0.433
Low RH	208	45.21	45.16	0.57	0.529
High RH	211	45.85	45.74	1.15	0.209
Low plus High RH	419	45.53	45.45	0.86	0.214

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	44.17		
Background RH	346	44.14	-0.03	0.971
Low RH	207	45.04	0.87	0.310
High RH	209	44.34	0.17	0.843
Low plus High RH	416	44.69	0.52	0.427

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-13. Analysis of ALT (U/L) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	43.54	0.005	0.012 (0.006)	0.059
Medium	256	44.75			
High	255	46.10			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of ALT versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	43.70	0.133	0.006 (0.007)	0.418
Medium	255	45.09			
High	252	45.45			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of ALT versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.4   ALT (Discrete)

No significant association with group or dioxin was revealed in any of the unadjusted or adjusted Model 1 through 4 analyses of ALT in its discrete form (Table 13-14(a-h): p>0.11 for each analysis).

Table 13-14. Analysis of ALT (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*54 (7.0)*	*0.92 (0.64,1.30)*	*0.625*
	Comparison	*1,154*	*88 (7.6)*		
Officer	Ranch Hand	305	21 (6.9)	1.28 (0.71,2.34)	0.414
	Comparison	459	25 (5.4)		
Enlisted Flyer	Ranch Hand	133	10 (7.5)	0.78 (0.35,1.77)	0.559
	Comparison	181	17 (9.4)		
Enlisted Groundcrew	Ranch Hand	330	23 (7.0)	0.76 (0.45,1.28)	0.307
	Comparison	514	46 (8.9)		

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Table 13-14. Analysis of ALT (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.93 (0.65,1.32)*	*0.670*
Officer	763	1.35 (0.73,2.47)	0.337
Enlisted Flyer	311	0.84 (0.37,1.94)	0.687
Enlisted Groundcrew	838	0.73 (0.43,1.24)	0.247

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

	Initial Dioxin Category Summary Statistics		Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	11 (8.0)	1.04 (0.80,1.34)	0.778
Medium	141	12 (8.5)		
High	140	12 (8.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.20 (0.85,1.70)	0.288

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	88 (7.6)		
Background RH	348	19 (5.5)	0.70 (0.42,1.17)	0.169
Low RH	208	19 (9.1)	1.22 (0.72,2.05)	0.456
High RH	211	16 (7.6)	1.00 (0.57,1.74)	0.990
Low plus High RH	419	35 (8.4)	1.10 (0.73,1.66)	0.646

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-14. Analysis of ALT (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	0.76 (0.44,1.29)	0.302
Low RH	207	1.24 (0.72,2.12)	0.438
High RH	209	0.79 (0.44,1.43)	0.436
Low plus High RH	416	0.99 (0.64,1.52)	0.958

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	13 (5.1)	1.15 (0.97,1.36)	0.112
Medium	256	19 (7.4)		
High	255	22 (8.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
762	1.12 (0.90,1.40)	0.313

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.5   GGT (Continuous)

All unadjusted and adjusted Model 1 through 4 analyses of GGT in its continuous form were nonsignificant (Table 13-15(a-h): p>0.07 for each analysis).

Table 13-15. Analysis of GGT (U/L) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*45.32*	*-0.10*	*0.929*
	Comparison	*1,154*	*45.41*		
Officer	Ranch Hand	305	43.72	0.56	0.741
	Comparison	459	43.16		
Enlisted Flyer	Ranch Hand	133	43.74	-2.14	0.425
	Comparison	181	45.87		
Enlisted Groundcrew	Ranch Hand	330	47.52	0.16	0.926
	Comparison	514	47.36		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*48.31*	*0.08*	*0.941*
	Comparison	*1,149*	*48.22*		
Officer	Ranch Hand	304	47.59	0.80	0.645
	Comparison	459	46.79		
Enlisted Flyer	Ranch Hand	132	48.34	-1.15	0.682
	Comparison	179	49.49		
Enlisted Groundcrew	Ranch Hand	327	48.56	-0.14	0.936
	Comparison	511	48.70		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 13-15. Analysis of GGT (U/L) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	47.53	47.58	0.001	-0.008 (0.019)	0.676
Medium	141	47.75	47.77			
High	140	47.78	47.71			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of GGT versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	51.01	0.120	-0.008 (0.022)	0.700
Medium	140	50.14			
High	138	50.72			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of GGT versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	45.41	45.40		
Background RH	348	42.61	42.90	-2.50	0.079
Low RH	208	47.15	47.04	1.64	0.368
High RH	211	48.22	47.90	2.50	0.172
Low plus High RH	419	47.69	47.47	2.07	0.135

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-15. Analysis of GGT (U/L) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	48.25		
Background RH	346	46.75	-1.50	0.311
Low RH	207	50.42	2.17	0.246
High RH	209	48.73	0.48	0.801
Low plus High RH	416	49.56	1.31	0.355

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	42.71	0.004	0.020 (0.011)	0.075
Medium	256	45.17			
High	255	48.24			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of GGT versus log$_2$ (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	44.96	0.115	0.005 (0.013)	0.668
Medium	255	48.02			
High	252	47.87			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of GGT versus log$_2$ (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.6   GGT (Discrete)

The unadjusted and adjusted Model 1 through 4 analyses of GGT in its discrete form were nonsignificant (Table 13-16(a-h): p>0.11 for each analysis).

Table 13-16. Analysis of GGT (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*77 (10.0)*	*0.90 (0.67,1.22)*	*0.494*
	Comparison	*1,154*	*127 (11.0)*		
Officer	Ranch Hand	305	30 (9.8)	1.06 (0.65,1.72)	0.829
	Comparison	459	43 (9.4)		
Enlisted Flyer	Ranch Hand	133	13 (9.8)	0.74 (0.36,1.53)	0.421
	Comparison	181	23 (12.7)		
Enlisted Groundcrew	Ranch Hand	330	34 (10.3)	0.85 (0.55,1.33)	0.483
	Comparison	514	61 (11.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.92 (0.67,1.25)*	*0.578*
Officer	763	1.09 (0.66,1.81)	0.727
Enlisted Flyer	311	0.81 (0.38,1.70)	0.577
Enlisted Groundcrew	838	0.83 (0.53,1.32)	0.432

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	19 (13.8)	0.83 (0.65,1.05)	0.112
Medium	141	17 (12.1)		
High	140	12 (8.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-16. Analysis of GGT (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	0.87 (0.63,1.21)	0.402

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	127 (11.0)		
Background RH	348	29 (8.3)	0.75 (0.49,1.15)	0.194
Low RH	208	27 (13.0)	1.20 (0.77,1.87)	0.429
High RH	211	21 (10.0)	0.87 (0.54,1.42)	0.588
Low plus High RH	419	48 (11.5)	1.02 (0.72,1.46)	0.907

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	0.81 (0.52,1.26)	0.352
Low RH	207	1.38 (0.87,2.19)	0.168
High RH	209	0.73 (0.43,1.23)	0.240
Low plus High RH	416	1.00 (0.69,1.45)	0.982

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-16. Analysis of GGT (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) High**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	256	24 (9.4)	1.02 (0.88,1.18)	0.798
Medium	256	27 (10.5)		
High	255	26 (10.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
762	1.02 (0.85,1.22)	0.850

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.7   Alkaline Phosphatase (Continuous)

The unadjusted Model 1 analysis of alkaline phosphatase revealed a significant difference between all Ranch Hands and Comparisons (Table 13-17(a): difference of means=2.26 U/L, p=0.048). After adjusting for covariates, the results became nonsignificant (Table 13-17(b): p=0.060). Stratifying by occupation showed no significant results in either the unadjusted or the adjusted Model 1 analyses (Table 13-17(a,b): p>0.05 for each analysis).

All unadjusted and adjusted Model 2 and 4 analyses of alkaline phosphatase were nonsignificant (Table 13-17(c,d,g,h): p>0.13 for each analysis).

The unadjusted Model 3 analysis of alkaline phosphatase revealed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 13-17(e): difference of means=3.69 U/L, p=0.048). Also in the unadjusted Model 3 analysis, a significant difference was seen between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-17(e): difference of means=3.34 U/L, p=0.018). After covariate adjustment, no contrasts were significant (Table 13-17(f): p>0.09 for each contrast).

Table 13-17. Analysis of Alkaline Phosphatase (U/L) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*94.58*	*2.26*	*0.048**
	Comparison	*1,154*	*92.32*		
Officer	Ranch Hand	305	89.72	1.06	0.537
	Comparison	459	88.66		
Enlisted Flyer	Ranch Hand	133	96.82	2.28	0.423
	Comparison	181	94.54		
Enlisted Groundcrew	Ranch Hand	330	98.37	3.46	0.052
	Comparison	514	94.92		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*766*	*94.88*	2.14	*0.060*
	Comparison	*1,150*	*92.74*		
Officer	Ranch Hand	304	90.83	1.18	0.496
	Comparison	459	89.65		
Enlisted Flyer	Ranch Hand	133	96.57	2.02	0.477
	Comparison	179	94.54		
Enlisted Groundcrew	Ranch Hand	329	97.33	3.11	0.077
	Comparison	512	94.22		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for $\log_2$ (Initial Dioxin)		
Initial Dioxin	**n**	**Unadjusted Mean[a]**	**Adjusted Mean[a,b]**	**R^2**	**Slope (Standard Error)[b,c]**	**p-Value**
Low	138	95.03	95.11	0.005	0.010 (0.010)	0.282
Medium	141	94.60	94.63			
High	140	96.91	96.80			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of alkaline phosphatase versus $\log_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (Initial Dioxin)		
Initial Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	138	92.58	0.041	-0.010 (0.011)	0.368
Medium	140	88.31			
High	140	87.88			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of alkaline phosphatase versus $\log_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	**n**	**Unadjusted Mean[a]**	**Adjusted Mean[a,b]**	**Difference of Adjusted Mean vs. Comparisons[b,c]**	**p-Value[d]**
Comparison	1,154	92.32	92.33		
Background RH	348	93.39	93.16	0.83	0.582
Low RH	208	95.24	95.32	2.99	0.108
High RH	211	95.78	96.02	3.69	0.048*
Low plus High RH	419	95.51	95.67	3.34	0.018*

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,150	92.67		
Background RH	347	95.06	2.39	0.117
Low RH	207	95.81	3.14	0.092
High RH	211	93.24	0.57	0.758
Low plus High RH	418	94.51	1.84	0.193

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	93.64	0.001	0.005 (0.006)	0.393
Medium	256	94.43			
High	255	95.56			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of alkaline phosphatase versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	92.95	0.047	-0.011 (0.007)	0.131
Medium	256	92.97			
High	254	88.88			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of alkaline phosphatase versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.8   Alkaline Phosphatase (Discrete)

The unadjusted and adjusted Model 1 analyses of alkaline phosphatase in its discrete form showed no significant overall group differences (Table 13-18(a,b): $p>0.07$ for each analysis). After stratifying by occupation, however, a significant difference was seen between Ranch Hands and Comparisons in the enlisted groundcrew stratum for both the unadjusted and adjusted analyses (Table 13-18(a,b): Unadjusted $RR=1.73$, $p=0.031$; Adjusted $RR=1.70$, $p=0.039$). Among the enlisted groundcrew, Ranch Hands had a higher percentage of abnormal alkaline phosphatase values than did the Comparisons (10.6% versus 6.4%).

All unadjusted and adjusted Models 2 through 4 analyses of alkaline phosphatase in its discrete form revealed no significant relation with dioxin (Table 13-18(c-h): $p>0.05$ for each analysis).

Table 13-18. Analysis of Alkaline Phosphatase (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High		Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*63*	*(8.2)*	*1.38 (0.97,1.97)*	*0.073*
	Comparison	*1,154*	*70*	*(6.1)*		
Officer	Ranch Hand	305	14	(4.6)	1.06 (0.52,2.12)	0.879
	Comparison	459	20	(4.4)		
Enlisted Flyer	Ranch Hand	133	14	(10.5)	1.13 (0.54,2.39)	0.739
	Comparison	181	17	(9.4)		
Enlisted Groundcrew	Ranch Hand	330	35	(10.6)	1.73 (1.05,2.84)	0.031*
	Comparison	514	33	(6.4)		

*: Statistically significant ($0.010<\text{p-value}\leq0.050$).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,916*	*1.37 (0.96,1.96)*	*0.086*
Officer	763	1.07 (0.53,2.16)	0.843
Enlisted Flyer	312	1.13 (0.53,2.40)	0.752
Enlisted Groundcrew	841	1.70 (1.03,2.80)	0.039*

*: Statistically significant ($0.010<\text{p-value}\leq0.050$).

Table 13-18. Analysis of Alkaline Phosphatase (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) High**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	138	9 (6.5)	1.17 (0.91,1.51)	0.217
Medium	141	11 (7.8)		
High	140	15 (10.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
418	1.06 (0.79,1.42)	0.701

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with an abnormally high alkaline phosphatase level.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	70 (6.1)		
Background RH	348	28 (8.0)	1.31 (0.83,2.08)	0.247
Low RH	208	15 (7.2)	1.21 (0.68,2.17)	0.511
High RH	211	20 (9.5)	1.67 (0.99,2.81)	0.055
Low plus High RH	419	35 (8.4)	1.43 (0.93,2.18)	0.103

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-18. Analysis of Alkaline Phosphatase (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,150		
Background RH	347	1.50 (0.93,2.41)	0.094
Low RH	207	1.26 (0.70,2.27)	0.442
High RH	211	1.33 (0.78,2.28)	0.298
Low plus High RH	418	1.30 (0.84,2.00)	0.241

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	19 (7.4)	1.01 (0.86,1.19)	0.861
Medium	256	22 (8.6)		
High	255	22 (8.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
765	0.92 (0.77,1.10)	0.356

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.9   Total Bilirubin (Continuous)

The unadjusted and adjusted Model 1 and 3 analyses of total bilirubin in its continuous form were nonsignificant (Table 13-19(a,b,e,f): p>0.15 for each analysis).

A significant inverse relation was seen between initial dioxin and total bilirubin in the unadjusted Model 2 analysis (Table 13-19(c): Slope=-0.035, p=0.044). After adjusting for covariates, the results were no longer significant (Table 13-19(d): p=0.844).

The unadjusted Model 4 analysis revealed a significant inverse relation between 1987 dioxin and total bilirubin (Table 13-19(g): Slope=-0.022, p=0.040). After covariate adjustment, the results became nonsignificant (Table 13-19(h): p=0.384).

Table 13-19. Analysis of Total Bilirubin (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*0.518*	*0.001*	*0.964*
	Comparison	*1,154*	*0.518*		
Officer	Ranch Hand	305	0.552	-0.006	0.779
	Comparison	459	0.557		
Enlisted Flyer	Ranch Hand	133	0.499	0.010	0.710
	Comparison	181	0.489		
Enlisted Groundcrew	Ranch Hand	330	0.496	0.002	0.908
	Comparison	514	0.494		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*0.493*	*0.003*	*0.754*
	Comparison	*1,149*	*0.489*		
Officer	Ranch Hand	304	0.507	-0.004	0.809
	Comparison	459	0.512		
Enlisted Flyer	Ranch Hand	132	0.485	0.016	0.551
	Comparison	179	0.470		
Enlisted Groundcrew	Ranch Hand	327	0.490	0.006	0.731
	Comparison	511	0.485		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 13-19. Analysis of Total Bilirubin (mg/dL) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	0.559	0.559	0.010	-0.035 (0.017)	0.044*
Medium	141	0.472	0.472			
High	140	0.500	0.500			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of total bilirubin versus log_2 (initial dioxin).

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	0.542	0.075	-0.004 (0.020)	0.844
Medium	140	0.484			
High	138	0.529			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of total bilirubin versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	0.518	0.518		
Background RH	348	0.530	0.531	0.013	0.394
Low RH	208	0.526	0.525	0.007	0.681
High RH	211	0.492	0.491	-0.027	0.154
Low plus High RH	419	0.509	0.508	-0.010	0.500

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-19. Analysis of Total Bilirubin (mg/dL) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	0.488		
Background RH	346	0.493	0.005	0.729
Low RH	207	0.501	0.013	0.464
High RH	209	0.481	-0.007	0.709
Low plus High RH	416	0.491	0.003	0.821

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	0.540	0.005	-0.022 (0.011)	0.040*
Medium	256	0.528			
High	255	0.488			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of total bilirubin versus log_2 (1987 dioxin).

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	0.520	0.048	-0.011 (0.013)	0.384
Medium	255	0.514			
High	252	0.484			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of total bilirubin versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.10 Total Bilirubin (Discrete)

All unadjusted and adjusted Model 1 through 4 analyses of total bilirubin in its discrete form were nonsignificant (Table 13-20(a-h): p>0.10 for each analysis).

Table 13-20. Analysis of Total Bilirubin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*50 (6.5)*	*0.99 (0.68,1.43)*	*0.948*
	Comparison	*1,154*	*76 (6.6)*		
Officer	Ranch Hand	305	22 (7.2)	1.04 (0.59,1.82)	0.899
	Comparison	459	32 (7.0)		
Enlisted Flyer	Ranch Hand	133	9 (6.8)	1.57 (0.59,4.18)	0.367
	Comparison	181	8 (4.4)		
Enlisted Groundcrew	Ranch Hand	330	19 (5.8)	0.81 (0.46,1.44)	0.475
	Comparison	514	36 (7.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*1.02 (0.70,1.48)*	*0.921*
Officer	763	1.06 (0.60,1.87)	0.838
Enlisted Flyer	311	1.62 (0.60,4.34)	0.342
Enlisted Groundcrew	838	0.84 (0.47,1.50)	0.553

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	14 (10.1)	0.77 (0.55,1.07)	0.101
Medium	141	5 (3.5)		
High	140	8 (5.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-20. Analysis of Total Bilirubin (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
416	0.92 (0.62,1.37)	0.674

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	76 (6.6)		
Background RH	348	23 (6.6)	1.01 (0.62,1.65)	0.957
Low RH	208	17 (8.2)	1.26 (0.73,2.18)	0.410
High RH	211	10 (4.7)	0.70 (0.36,1.38)	0.302
Low plus High RH	419	27 (6.4)	0.94 (0.59,1.49)	0.784

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	1.05 (0.64,1.74)	0.837
Low RH	207	1.37 (0.78,2.40)	0.272
High RH	209	0.70 (0.35,1.42)	0.324
Low plus High RH	416	0.98 (0.61,1.58)	0.928

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-20. Analysis of Total Bilirubin (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	16 (6.3)	0.95 (0.80,1.14)	0.599
Medium	256	21 (8.2)		
High	255	13 (5.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
762	0.98 (0.79,1.23)	0.883

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.11   Direct Bilirubin (Discrete)

Because of a sparse number of participants with abnormally high direct bilirubin values, the analysis was limited for some of the models.

The unadjusted Model 1 analysis revealed no significant group differences (Table 13-21(a): p>0.05 for each analysis). After adjusting for covariates, a significant overall group difference was seen (Table 13-21(b): Adjusted RR=0.24, p=0.041). The percentage of Ranch Hands with abnormally high direct bilirubin values was 0.3 percent versus 1.0 percent for Comparisons. After stratifying by military occupation, no significant difference between Ranch Hands and Comparisons was seen among officers (Table 13-21(b): p=0.401). No adjusted Model 1 analyses were performed for enlisted flyers and enlisted groundcrew due to a sparse number of abnormalities.

No Model 2 analyses were performed because there were no abnormally high direct bilirubin values for Ranch Hands with an extrapolated initial dioxin level. All unadjusted and adjusted Model 3 and 4 analyses of direct bilirubin were nonsignificant (Table 13-21(e-h): p>0.09 for each analysis).

Table 13-21. Analysis of Direct Bilirubin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*2 (0.3)*	*0.27 (0.06,1.23)*	*0.053*
	Comparison	*1,154*	*11 (1.0)*		
Officer	Ranch Hand	305	2 (0.7)	0.60 (0.12,3.11)	0.542
	Comparison	459	5 (1.1)		
Enlisted Flyer	Ranch Hand	133	0 (0.0)	--	--
	Comparison	181	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	330	0 (0.0)	--	0.121[a]
	Comparison	514	6 (1.2)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormally high direct bilirubin level.

--: Results were not presented because of the sparse number of participants with an abnormally high direct bilirubin level.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.24 (0.05,1.14)*	*0.041**
Officer	763	0.48 (0.09,2.67)	0.401
Enlisted Flyer	311	--	--
Enlisted Groundcrew	838	--	--

--: Results were not presented because of the sparse number of participants with an abnormally high direct bilirubin level.

*: Statistically significant (0.010<p-value≤0.050).

Note: Results were not adjusted for military occupation because of the sparse number of participants with an abnormally high direct bilirubin level.

Table 13-21. Analysis of Direct Bilirubin (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) High**	**Unadjusted Relative Risk (95% C.I.)**	**p-Value**
Low	138	0 (0.0)	--	--
Medium	141	0 (0.0)		
High	140	0 (0.0)		

--: Analysis was not performed because there were no abnormally high direct bilirubin values for Ranch Hands with an extrapolated initial dioxin level.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
416	--	--

--: Analysis was not performed because there were no abnormally high direct bilirubin values for Ranch Hands with an extrapolated initial dioxin level.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	11 (1.0)		
Background RH	348	2 (0.6)	0.69 (0.15,3.17)	0.635
Low RH	208	0 (0.0)	--	0.321[c]
High RH	211	0 (0.0)	--	0.315[c]
Low plus High RH	419	0 (0.0)	--	0.096[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormally high direct bilirubin level.

--: Results were not presented because of the sparse number of participants with an abnormally high direct bilirubin level.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-21. Analysis of Direct Bilirubin (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	0.64 (0.13,3.27)	0.592
Low RH	207	--	--
High RH	209	--	--
Low plus High RH	416	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with an abnormally high direct bilirubin level.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for military occupation because of the sparse number of participants with an abnormally high direct bilirubin level.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	1 (0.4)	0.50 (0.21,1.17)	0.124
Medium	256	1 (0.4)		
High	255	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
762	0.53 (0.20,1.40)	0.191

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, military occupation, cumulative degreasing chemical exposure, and current cigarette smoking because of the sparse number of Ranch Hands with an abnormally high direct bilirubin level.

13.2.2.3.12   LDH (Continuous)

The unadjusted and adjusted Model 1 analyses of LDH in its continuous form showed no significant overall group differences (Table 13-22(a,b): p>0.08 for each analysis). Stratifying by military occupation in the unadjusted Model 1 analysis revealed a significant difference between Ranch Hands and Comparisons among officers (Table 13-22(a): difference of means=4.1 U/L, p=0.049). After adjusting for covariates, no significant group differences were seen in any of the occupational strata (Table 13-22(b): p>0.05 for each analysis).

All unadjusted and adjusted analyses of LDH in Models 2 through 4 were nonsignificant (Table 13-22(c-h): p>0.07 for each analysis).

Table 13-22. Analysis of LDH (U/L) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*154.1*	*2.2*	*0.089*
	Comparison	*1,154*	*151.9*		
Officer	Ranch Hand	305	155.8	4.1	0.049*
	Comparison	459	151.7		
Enlisted Flyer	Ranch Hand	133	152.1	0.4	0.892
	Comparison	181	151.7		
Enlisted Groundcrew	Ranch Hand	330	153.4	1.2	0.531
	Comparison	514	152.1		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*155.7*	*2.2*	*0.081*
	Comparison	*1,149*	*153.5*		
Officer	Ranch Hand	304	157.0	3.9	0.053
	Comparison	459	153.1		
Enlisted Flyer	Ranch Hand	132	152.9	0.3	0.917
	Comparison	179	152.5		
Enlisted Groundcrew	Ranch Hand	327	156.6	1.4	0.468
	Comparison	511	155.2		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 13-22. Analysis of LDH (U/L) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	159.5	159.6	0.008	-0.011 (0.007)	0.085
Medium	141	149.8	149.8			
High	140	154.2	154.1			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of LDH versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	158.1	0.060	-0.001 (0.008)	0.868
Medium	140	151.5			
High	138	157.9			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of LDH versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	151.9	151.8		
Background RH	348	153.8	154.7	2.9	0.094
Low RH	208	155.9	155.5	3.7	0.078
High RH	211	153.0	152.2	0.4	0.878
Low plus High RH	419	154.4	153.8	2.0	0.210

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-22. Analysis of LDH (U/L) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	153.6		
Background RH	346	156.4	2.8	0.103
Low RH	207	155.5	1.9	0.346
High RH	209	154.7	1.1	0.608
Low plus High RH	416	155.1	1.5	0.337

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented
  because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	153.1	<0.001	-0.001 (0.004)	0.879
Medium	256	157.6			
High	255	151.8			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of LDH versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	154.8	0.026	-0.002 (0.005)	0.685
Medium	255	157.5			
High	252	152.2			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of LDH versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.13   LDH (Discrete)

No significant relations between LDH in its discrete form and either group or dioxin were seen in the unadjusted and adjusted Model 1, 3, and 4 analyses (Table 13-23(a,b,e-h): p>0.08 for each analysis).

The unadjusted Model 2 analysis revealed a significant inverse relation between initial dioxin and LDH (Table 13-23(c): Unadjusted RR=0.76, p=0.028). After covariate adjustment, the results became nonsignificant (Table 13-22(d): p=0.240).

Table 13-23. Analysis of LDH (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*85 (11.1)*	*1.21 (0.89,1.63)*	*0.224*
	Comparison	*1,154*	*108 (9.4)*		
Officer	Ranch Hand	305	39 (12.8)	1.46 (0.92,2.31)	0.111
	Comparison	459	42 (9.2)		
Enlisted Flyer	Ranch Hand	133	17 (12.8)	1.51 (0.73,3.11)	0.263
	Comparison	181	16 (8.8)		
Enlisted Groundcrew	Ranch Hand	330	29 (8.8)	0.89 (0.55,1.44)	0.648
	Comparison	514	50 (9.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*1.25 (0.92,1.70)*	*0.159*
Officer	763	1.44 (0.90,2.31)	0.125
Enlisted Flyer	311	1.58 (0.75,3.30)	0.228
Enlisted Groundcrew	838	0.96 (0.59,1.58)	0.885

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	21 (15.2)	0.76 (0.58,0.98)	0.028*
Medium	141	13 (9.2)		
High	140	11 (7.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-23. Analysis of LDH (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
416	0.84 (0.62,1.13)	0.240

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	108 (9.4)		
Background RH	348	40 (11.5)	1.40 (0.95,2.07)	0.088
Low RH	208	27 (13.0)	1.40 (0.89,2.20)	0.150
High RH	211	18 (8.5)	0.82 (0.48,1.39)	0.458
Low plus High RH	419	45 (10.7)	1.07 (0.73,1.56)	0.735

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	1.42 (0.95,2.13)	0.086
Low RH	207	1.28 (0.80,2.03)	0.301
High RH	209	0.94 (0.54,1.62)	0.822
Low plus High RH	416	1.09 (0.74,1.61)	0.647

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-23. Analysis of LDH (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) High**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	256	25 (9.8)	0.94 (0.82,1.08)	0.400
Medium	256	40 (15.6)		
High	255	20 (7.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
762	0.90 (0.76,1.08)	0.257

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.14 Cholesterol (Continuous)

No significant associations between group or dioxin and cholesterol in its continuous form were seen in the unadjusted and adjusted Model 1, 2, and 4 analyses (Table 13-24(a-d, g,h): p>0.10 for each analysis).

A significant difference between Ranch Hands in the background dioxin category and Comparisons was revealed in the unadjusted Model 3 analysis (Table 13-24(e): difference of adjusted means=-4.7 mg/dL, p=0.035). All other unadjusted contrasts were nonsignificant (Table 13-24(e): p≥0.34 for each contrast). After covariate adjustment all contrasts were nonsignificant (Table 13-24(f): p>0.14 for each contrast).

Table 13-24. Analysis of Cholesterol (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*194.8*	*-2.8*	*0.102*
	Comparison	*1,154*	*197.6*		
Officer	Ranch Hand	305	190.7	-4.0	0.132
	Comparison	459	194.7		
Enlisted Flyer	Ranch Hand	133	196.4	-2.2	0.604
	Comparison	181	198.6		
Enlisted Groundcrew	Ranch Hand	330	198.0	-1.8	0.481
	Comparison	514	199.8		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*196.3*	*-2.5*	*0.133*
	Comparison	*1,149*	*198.8*		
Officer	Ranch Hand	304	193.7	-3.3	0.207
	Comparison	459	197.1		
Enlisted Flyer	Ranch Hand	132	199.1	-2.4	0.558
	Comparison	179	201.5		
Enlisted Groundcrew	Ranch Hand	327	196.2	-1.8	0.478
	Comparison	511	198.0		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Table 13-24. Analysis of Cholesterol (mg/dL) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	190.9	190.3	0.042	0.026 (0.047)	0.586
Medium	141	197.3	197.1			
High	140	195.9	196.7			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of cholesterol versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	192.0	0.082	-0.014 (0.055)	0.797
Medium	140	196.5			
High	138	195.9			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of cholesterol versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	197.6	197.7		
Background RH	348	195.0	193.0	-4.7	0.035*
Low RH	208	194.4	195.1	-2.6	0.340
High RH	211	195.1	196.9	-0.8	0.777
Low plus High RH	419	194.7	196.0	-1.7	0.417

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-24. Analysis of Cholesterol (mg/dL) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	199.1		
Background RH	346	196.4	-2.7	0.230
Low RH	207	197.2	-1.9	0.499
High RH	209	195.1	-4.0	0.148
Low plus High RH	416	196.2	-2.9	0.158

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	195.6	<0.001	-0.001 (0.029)	0.979
Medium	256	193.5			
High	255	195.4			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of cholesterol versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	198.0	0.076	-0.014 (0.033)	0.672
Medium	255	198.1			
High	252	194.8			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of cholesterol versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.15 Cholesterol (Discrete)

All unadjusted and adjusted Model 1, 2, and 4 analyses of cholesterol in its discrete form were nonsignificant (Table 13-25(a-d,g,h): p>0.08 for each analysis).

The unadjusted Model 3 analysis revealed no significant differences between dioxin categories (Table 13-25(e): p≥0.16 for each contrast). Adjustment for covariates revealed a significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-25(f): Adjusted RR=0.68, p=0.039). Ranch Hands in the low and high dioxin categories combined had a smaller percentage of abnormally high cholesterol values than Comparisons (10.3% versus 13.3%). All remaining contrasts were nonsignificant (Table 13-25(f): p>0.06 for each contrast).

Table 13-25. Analysis of Cholesterol (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*83 (10.8)*	*0.79 (0.59,1.05)*	*0.095*
	Comparison	*1,154*	*154 (13.3)*		
Officer	Ranch Hand	305	23 (7.5)	0.75 (0.44,1.27)	0.283
	Comparison	459	45 (9.8)		
Enlisted Flyer	Ranch Hand	133	18 (13.5)	1.02 (0.53,1.97)	0.944
	Comparison	181	24 (13.3)		
Enlisted Groundcrew	Ranch Hand	330	42 (12.7)	0.74 (0.49,1.10)	0.132
	Comparison	514	85 (16.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.78 (0.58,1.04)*	*0.088*
Officer	763	0.78 (0.46,1.33)	0.369
Enlisted Flyer	311	0.96 (0.49,1.89)	0.908
Enlisted Groundcrew	838	0.72 (0.48,1.08)	0.112

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	10 (7.2)	1.06 (0.83,1.34)	0.659
Medium	141	18 (12.8)		
High	140	15 (10.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-25. Analysis of Cholesterol (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.08 (0.80,1.46)	0.635

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	154 (13.3)		
Background RH	348	40 (11.5)	0.78 (0.53,1.13)	0.184
Low RH	208	20 (9.6)	0.70 (0.43,1.15)	0.160
High RH	211	23 (10.9)	0.85 (0.53,1.36)	0.502
Low plus High RH	419	43 (10.3)	0.77 (0.54,1.11)	0.164

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	0.90 (0.61,1.32)	0.581
Low RH	207	0.73 (0.44,1.21)	0.222
High RH	209	0.63 (0.38,1.02)	0.063
Low plus High RH	416	0.68 (0.47,0.98)	0.039*

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

*: Statistically significant ($0.010 <$ p-value ≤ 0.050).

Table 13-25. Analysis of Cholesterol (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	30 (11.7)	0.98 (0.85,1.13)	0.740
Medium	256	25 (9.8)		
High	255	28 (11.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
762	0.94 (0.80,1.10)	0.435

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.16   HDL Cholesterol (Continuous)

No significant group differences were seen in the unadjusted and adjusted Model 1 analyses of HDL cholesterol in its continuous form (Table 13-26(a,b): p≥0.27 for each analysis).

As initial dioxin increased, a significant decrease in HDL cholesterol was observed in the unadjusted Model 2 analysis (Table 13-26(c): Slope=-0.024, p=0.012). The results of the adjusted Model 2 analysis were nonsignificant (Table 13-26(d): p=0.494).

The unadjusted Model 3 analysis revealed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 13-26(e): difference of means=-2.55 mg/dL, p=0.002), as well as a significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-26(e): difference of means=-1.34 mg/dL, p=0.035). After covariate adjustment, no contrasts were significant (Table 13-26(f): p>0.20 for each contrast).

As 1987 dioxin increased, a significant decrease in HDL cholesterol was observed in the unadjusted Model 4 analysis (Table 13-26(g): Slope=-0.031, p<0.001). The results were no longer significant after adjusting for covariates (Table 13-26(h): p=0.693).

Table 13-26. Analysis of HDL Cholesterol (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*44.35*	*-0.25*	*0.643*
	Comparison	*1,154*	*44.60*		
Officer	Ranch Hand	305	47.22	0.21	0.814
	Comparison	459	47.01		
Enlisted Flyer	Ranch Hand	133	43.51	0.30	0.818
	Comparison	181	43.21		
Enlisted Groundcrew	Ranch Hand	330	42.18	-0.86	0.270
	Comparison	514	43.04		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*46.56*	*-0.17*	*0.748*
	Comparison	*1,149*	*46.72*		
Officer	Ranch Hand	304	48.66	0.25	0.770
	Comparison	459	48.42		
Enlisted Flyer	Ranch Hand	132	46.15	0.35	0.780
	Comparison	179	45.81		
Enlisted Groundcrew	Ranch Hand	327	45.10	-0.72	0.347
	Comparison	511	45.82		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 13-26. Analysis of HDL Cholesterol (mg/dL) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	45.42	45.19	0.075	-0.024 (0.009)	0.012*
Medium	141	41.19	41.12			
High	140	41.77	42.05			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of HDL cholesterol versus log_2 (initial dioxin).

*: Statistically significant ($0.010 < $ p-value $ \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	46.66	0.238	-0.007 (0.010)	0.494
Medium	140	43.55			
High	138	45.18			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of HDL cholesterol versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-26. Analysis of HDL Cholesterol (mg/dL) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	44.60	44.65		
Background RH	348	46.33	45.41	0.76	0.279
Low RH	208	44.25	44.57	-0.08	0.925
High RH	211	41.29	42.10	-2.55	0.002**
Low plus High RH	419	42.74	43.31	-1.34	0.035*

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

  *: Statistically significant ($0.010 < $p-value$ \leq 0.050$).
**: Statistically significant (p-value≤ 0.010).

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	46.69		
Background RH	346	46.78	0.09	0.894
Low RH	207	46.91	0.22	0.785
High RH	209	45.62	-1.07	0.209
Low plus High RH	416	46.26	-0.43	0.504

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-26. Analysis of HDL Cholesterol (mg/dL) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	256	47.04	0.032	-0.031 (0.006)	<0.001**
Medium	256	44.90			
High	255	41.23			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of HDL cholesterol versus log_2 (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	255	46.34	0.206	-0.003 (0.007)	0.693
Medium	255	46.74			
High	252	44.42			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of HDL cholesterol versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.17 HDL Cholesterol (Discrete)

All unadjusted and adjusted Model 1 through 4 analyses of HDL cholesterol in its discrete form were nonsignificant (Table 13-27(a-h): p>0.05 for each analysis).

Table 13-27. Analysis of HDL Cholesterol (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*139 (18.1)*	*1.25 (0.98,1.60)*	*0.072*
	Comparison	*1,154*	*173 (15.0)*		
Officer	Ranch Hand	305	47 (15.4)	1.49 (0.97,2.29)	0.068
	Comparison	459	50 (10.9)		
Enlisted Flyer	Ranch Hand	133	23 (17.3)	0.97 (0.54,1.76)	0.929
	Comparison	181	32 (17.7)		
Enlisted Groundcrew	Ranch Hand	330	69 (20.9)	1.23 (0.87,1.74)	0.247
	Comparison	514	91 (17.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*1.25 (0.97,1.62)*	*0.086*
Officer	763	1.52 (0.98,2.36)	0.064
Enlisted Flyer	311	0.93 (0.50,1.73)	0.825
Enlisted Groundcrew	838	1.22 (0.85,1.76)	0.289

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	20 (14.5)	1.04 (0.87,1.25)	0.660
Medium	141	36 (25.5)		
High	140	26 (18.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	0.91 (0.73,1.12)	0.366

[a]Relative risk for a twofold increase in initial dioxin.

Table 13-27. Analysis of HDL Cholesterol (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	173 (15.0)		
Background RH	348	57 (16.4)	1.26 (0.91,1.76)	0.167
Low RH	208	37 (17.8)	1.18 (0.79,1.76)	0.414
High RH	211	45 (21.3)	1.39 (0.96,2.03)	0.081
Low plus High RH	419	82 (19.6)	1.28 (0.95,1.73)	0.099

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	1.41 (0.99,2.00)	0.055
Low RH	207	1.15 (0.76,1.75)	0.496
High RH	209	1.18 (0.80,1.76)	0.407
Low plus High RH	416	1.17 (0.86,1.59)	0.323

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	40 (15.6)	1.07 (0.95,1.19)	0.271
Medium	256	40 (15.6)		
High	255	59 (23.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 13-27. Analysis of HDL Cholesterol (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
762	0.93 (0.81,1.07)	0.334

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.18   Cholesterol-HDL Ratio (Continuous)

No significant group differences were seen in the unadjusted and adjusted Model 1 analyses of cholesterol-HDL ratio (Table 13-28(a,b): p>0.22 for each analysis).

The unadjusted Model 2 analysis revealed a significant positive association between initial dioxin and cholesterol-HDL ratio (Table 13-28(c): Slope=0.027, p=0.009). The relation was no longer significant after adjusting for covariates (Table 13-28(d): p=0.692).

The unadjusted Model 3 analysis revealed a significant difference between Ranch Hands in the background dioxin category and Comparisons (Table 13-28(e): difference of means=-0.17, p=0.020) as well as a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 13-28(e): difference of means=0.24, p=0.010). After covariate adjustment, however, all contrasts were nonsignificant (Table 13-28(f): p>0.35 for each contrast).

A significant positive association was revealed between 1987 dioxin and cholesterol-HDL ratio in the unadjusted Model 4 analysis (Table 13-28(g): Slope=0.030, p<0.001). The adjusted Model 4 analysis results were nonsignificant (Table 13-28(h): p=0.956).

Table 13-28. Analysis of Cholesterol-HDL Ratio (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*4.36*	*-0.04*	*0.543*
	Comparison	*1,154*	*4.39*		
Officer	Ranch Hand	305	4.01	-0.10	0.228
	Comparison	459	4.11		
Enlisted Flyer	Ranch Hand	133	4.48	-0.08	0.574
	Comparison	181	4.56		
Enlisted Groundcrew	Ranch Hand	330	4.65	0.05	0.556
	Comparison	514	4.60		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 13-28. Analysis of Cholesterol-HDL Ratio (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*4.18*	*-0.04*	*0.482*
	Comparison	*1,149*	*4.21*		
Officer	Ranch Hand	304	3.95	-0.09	0.274
	Comparison	459	4.03		
Enlisted Flyer	Ranch Hand	132	4.27	-0.09	0.515
	Comparison	179	4.36		
Enlisted Groundcrew	Ranch Hand	327	4.31	0.03	0.699
	Comparison	511	4.28		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	4.17	4.18	0.025	0.027 (0.010)	0.009**
Medium	141	4.75	4.75			
High	140	4.65	4.63			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of cholesterol-HDL ratio versus $\log_2$ (initial dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	4.08	0.153	0.005 (0.012)	0.692
Medium	140	4.47			
High	138	4.29			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of cholesterol-HDL ratio versus $\log_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-28. Analysis of Cholesterol-HDL Ratio (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	4.39	4.39		
Background RH	348	4.17	4.22	-0.17	0.020*
Low RH	208	4.36	4.34	-0.05	0.627
High RH	211	4.68	4.63	0.24	0.010**
Low plus High RH	419	4.52	4.49	0.10	0.163

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented
  because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	4.22		
Background RH	346	4.16	-0.06	0.359
Low RH	207	4.17	-0.05	0.513
High RH	209	4.23	0.01	0.889
Low plus High RH	416	4.20	-0.02	0.740

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented
  because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-28. Analysis of Cholesterol-HDL Ratio (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	4.12	0.028	0.030 (0.006)	<0.001**
Medium	256	4.27			
High	255	4.70			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of cholesterol-HDL ratio versus log_2 (1987 dioxin).

**: Statistically significant (p-value$\leq$0.010).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	4.23	0.145	0.000 (0.007)	0.956
Medium	255	4.20			
High	252	4.34			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of cholesterol-HDL ratio versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.19   Cholesterol-HDL Ratio (Discrete)

The unadjusted and adjusted Model 1 and 2 analyses of cholesterol-HDL ratio in its discrete form were nonsignificant (Table 13-29(a-d): p>0.16 for each analysis).

A significant difference between Ranch Hands in the background dioxin category and Comparisons was revealed in the unadjusted Model 3 analysis (Table 13-29(e): Unadjusted RR=0.76, p=0.045). The remaining unadjusted contrasts were nonsignificant (Table 13-29(e): p$\geq$0.07 for each contrast). The adjusted Model 3 analysis revealed no significant relation between dioxin category and dichotomized cholesterol-HDL ratio (Table 13-29(f): p$\geq$0.28 for each contrast).

The unadjusted Model 4 analysis revealed a significant positive relation between 1987 dioxin and cholesterol-HDL ratio (Table 13-29(g): Unadjusted RR=1.17, p<0.001). The relation was no longer significant after adjusting for covariates (Table 13-29(h): p=0.866).

Table 13-29. Analysis of Cholesterol-HDL Ratio (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*241 (31.4)*	*0.95 (0.78,1.16)*	*0.608*
	Comparison	*1,154*	*375 (32.5)*		
Officer	Ranch Hand	305	67 (22.0)	0.87 (0.62,1.23)	0.437
	Comparison	459	112 (24.4)		
Enlisted Flyer	Ranch Hand	133	42 (31.6)	0.79 (0.49,1.26)	0.318
	Comparison	181	67 (37.0)		
Enlisted Groundcrew	Ranch Hand	330	132 (40.0)	1.08 (0.81,1.44)	0.587
	Comparison	514	196 (38.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.94 (0.76,1.15)*	*0.537*
Officer	763	0.88 (0.62,1.25)	0.481
Enlisted Flyer	311	0.77 (0.47,1.26)	0.305
Enlisted Groundcrew	838	1.05 (0.78,1.41)	0.745

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	36 (26.1)	1.11 (0.96,1.29)	0.163
Medium	141	63 (44.7)		
High	140	52 (37.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	0.93 (0.77,1.12)	0.430

[a]Relative risk for a twofold increase in initial dioxin.

Table 13-29. Analysis of Cholesterol-HDL Ratio (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	375 (32.5)		
Background RH	348	90 (25.9)	0.76 (0.58,0.99)	0.045*
Low RH	208	67 (32.2)	0.97 (0.71,1.34)	0.870
High RH	211	84 (39.8)	1.32 (0.98,1.79)	0.070
Low plus High RH	419	151 (36.0)	1.14 (0.90,1.44)	0.288

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	0.85 (0.64,1.14)	0.280
Low RH	207	0.98 (0.71,1.37)	0.925
High RH	209	1.00 (0.72,1.38)	0.998
Low plus High RH	416	0.99 (0.77,1.27)	0.951

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	61 (23.8)	1.17 (1.07,1.29)	<0.001**
Medium	256	76 (29.7)		
High	255	104 (40.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 13-29. Analysis of Cholesterol-HDL Ratio (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
762	0.99 (0.88,1.11)	0.866

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.20 Triglycerides (Continuous)

No significant association with group or dioxin was revealed in the unadjusted and adjusted Model 1 and 2 analyses of triglycerides in its continuous form (Table 13-30(a-d): p>0.08 for each analysis).

The Model 3 unadjusted analysis revealed three significant contrasts: Ranch Hands in the background dioxin category versus Comparisons (Table 13-30(e): difference of means=-8.2 mg/dL, p=0.045), Ranch Hands in the high dioxin category versus Comparisons (Table 13-30(e): difference of means=16.6 mg/dL, p=0.002), and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-30(e): difference of means=10.6 mg/dL). After covariate adjustment, all contrasts were nonsignificant (Table 13-30(f): p>0.21 for each contrast).

The unadjusted Model 4 analysis revealed a significant relation between triglycerides in its continuous form and 1987 dioxin (Table 13-30(g): Slope=0.060, p<0.001). After adjusting for covariates, however, the results were nonsignificant (Table 13-30(h): p=0.077).

Table 13-30. Analysis of Triglycerides (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*134.8*	*1.3*	*0.695*
	Comparison	*1,154*	*133.5*		
Officer	Ranch Hand	305	122.8	0.7	0.876
	Comparison	459	122.1		
Enlisted Flyer	Ranch Hand	133	140.1	-2.7	0.746
	Comparison	181	142.8		
Enlisted Groundcrew	Ranch Hand	330	144.5	3.4	0.516
	Comparison	514	141.1		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 13-30. Analysis of Triglycerides (mg/dL) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*117.6*	*0.9*	*0.743*
	Comparison	*1,149*	*116.7*		
Officer	Ranch Hand	304	109.8	1.3	0.746
	Comparison	459	108.5		
Enlisted Flyer	Ranch Hand	132	122.4	-1.8	0.800
	Comparison	179	124.1		
Enlisted Groundcrew	Ranch Hand	327	120.2	1.4	0.733
	Comparison	511	118.8		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	132.0	132.5	0.018	0.036 (0.021)	0.084
Medium	141	153.7	154.0			
High	140	153.3	152.4			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of triglycerides versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	119.2	0.082	0.024 (0.024)	0.329
Medium	140	133.5			
High	138	133.7			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of triglycerides versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-30. Analysis of Triglycerides (mg/dL) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	133.5	133.3		
Background RH	348	122.4	125.1	-8.2	0.045*
Low RH	208	139.2	138.2	4.9	0.357
High RH	211	153.1	149.9	16.6	0.002**
Low plus High RH	419	146.1	143.9	10.6	0.009**

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	117.0		
Background RH	346	113.6	-3.4	0.344
Low RH	207	120.8	3.8	0.402
High RH	209	121.7	4.7	0.308
Low plus High RH	416	121.3	4.3	0.218

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-30. Analysis of Triglycerides (mg/dL) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	256	119.7	0.031	0.060 (0.012)	<0.001**
Medium	256	132.1			
High	255	155.0			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of triglycerides versus log$_2$ (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	255	114.0	0.101	0.025 (0.014)	0.077
Medium	255	120.1			
High	252	130.3			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of triglycerides versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.21 Triglycerides (Discrete)

A significant difference between Ranch Hands and Comparisons was seen in the unadjusted and adjusted Model 1 analyses of triglycerides in its dichotomized form (Table 13-31(a,b): Unadjusted RR=1.43, p=0.015; Adjusted RR=1.40, p=0.023). In each of the unadjusted and adjusted Model 1 analyses, stratifying by military occupation revealed a significant difference between Ranch Hands and Comparisons among enlisted groundcrew (Table 13-31(a,b): Unadjusted RR=1.62, p=0.015; Adjusted RR=1.54, p=0.034). For all participants, Ranch Hands had a higher percentage of abnormal triglyceride values than Comparisons (13.4% versus 9.8%). Among enlisted groundcrew, 17.9 percent of Ranch Hands had abnormal triglyceride values versus 11.9 percent of Comparisons.

No significant association was seen between initial dioxin and triglycerides in the unadjusted and adjusted Model 2 analyses (Table 13-31(c,d): p>0.09 for each analysis).

The unadjusted Model 3 analysis of triglycerides revealed three significant contrasts: Ranch Hands in the low dioxin category versus Comparisons, Ranch Hands in the high dioxin category versus Comparisons, and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-31(e): Unadjusted RR=1.65, p=0.021; Unadjusted RR=2.26, p<0.001; Unadjusted RR =1.93, p<0.001,

respectively). These same contrasts were significant in the adjusted Model 3 analysis: (Table 13-31(f): Adjusted RR=1.72, p=0.015 for Ranch Hands in the low dioxin category versus Comparisons; Adjusted RR=1.70, p=0.012 for Ranch Hands in the high dioxin category versus Comparisons; Adjusted RR=1.71, p=0.001 for Ranch Hands in the low and high dioxin categories combined). The percentages of Ranch Hands with abnormal triglyceride values in the low dioxin category, high dioxin category, and low and high dioxin categories combined were 15.4, 20.4, and 17.9, respectively, versus 9.8 percent for Comparisons.

A significant positive association between 1987 dioxin and dichotomized triglycerides was revealed in each of the unadjusted and adjusted Model 4 analyses (Table 13-31(g,h): Unadjusted RR=1.35, p<0.001; Adjusted RR=1.20, p=0.020). The percentages of abnormally high triglyceride values in the low, medium, and high 1987 dioxin categories were 6.3, 12.9, and 21.2, respectively.

Table 13-31. Analysis of Triglycerides (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*103 (13.4)*	*1.43 (1.07,1.90)*	*0.015**
	Comparison	*1,154*	*113 (9.8)*		
Officer	Ranch Hand	305	26 (8.5)	1.20 (0.70,2.06)	0.499
	Comparison	459	33 (7.2)		
Enlisted Flyer	Ranch Hand	133	18 (13.5)	1.33 (0.67,2.65)	0.411
	Comparison	181	19 (10.5)		
Enlisted Groundcrew	Ranch Hand	330	59 (17.9)	1.62 (1.10,2.38)	0.015*
	Comparison	514	61 (11.9)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*1.40 (1.05,1.88)*	*0.023**
Officer	763	1.22 (0.71,2.09)	0.474
Enlisted Flyer	311	1.34 (0.66,2.70)	0.415
Enlisted Groundcrew	838	1.54 (1.03,2.29)	0.034*

*: Statistically significant (0.010<p-value≤0.050).

Table 13-31. Analysis of Triglycerides (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	17 (12.3)	1.17 (0.97,1.40)	0.099
Medium	141	28 (19.9)		
High	140	30 (21.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.06 (0.85,1.33)	0.577

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	113 (9.8)		
Background RH	348	28 (8.0)	0.85 (0.55,1.31)	0.461
Low RH	208	32 (15.4)	1.65 (1.08,2.52)	0.021*
High RH	211	43 (20.4)	2.26 (1.53,3.34)	<0.001**
Low plus High RH	419	75 (17.9)	1.93 (1.40,2.66)	<0.001**

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-31. Analysis of Triglycerides (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	0.96 (0.61,1.50)	0.845
Low RH	207	1.72 (1.11,2.66)	0.015*
High RH	209	1.70 (1.12,2.57)	0.012*
Low plus High RH	416	1.71 (1.23,2.38)	0.001**

[a]Relative risk and confidence interval relative to Comparisons.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	16 (6.3)	1.35 (1.18,1.53)	<0.001**
Medium	256	33 (12.9)		
High	255	54 (21.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
762	1.20 (1.03,1.40)	0.020*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

13.2.2.3.22   Creatine Phosphokinase (Continuous)

The unadjusted and adjusted Model 1, 2, and 3 analyses of creatine phosphokinase in its continuous form were nonsignificant (Table 13-32(a-f): p>0.18 for each analysis).

A significant positive association was seen between 1987 dioxin and creatine phosphokinase in the unadjusted Model 4 analysis (Table 13-32(g): Slope=0.028, p=0.032). The results of the adjusted Model 4 analysis were nonsignificant (Table 13-32(h): p=0.654).

Table 13-32. Analysis of Creatine Phosphokinase (U/L) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*107.6*	*1.3*	*0.672*
	Comparison	*1,154*	*106.3*		
Officer	Ranch Hand	305	104.0	1.6	0.725
	Comparison	459	102.4		
Enlisted Flyer	Ranch Hand	133	97.0	-7.4	0.286
	Comparison	181	104.3		
Enlisted Groundcrew	Ranch Hand	330	115.7	5.1	0.290
	Comparison	514	110.7		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*142.1*	*2.7*	*0.472*
	Comparison	*1,149*	*139.4*		
Officer	Ranch Hand	304	144.2	1.9	0.750
	Comparison	459	142.3		
Enlisted Flyer	Ranch Hand	132	131.2	-7.7	0.379
	Comparison	179	138.9		
Enlisted Groundcrew	Ranch Hand	327	147.8	7.6	0.185
	Comparison	511	140.1		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 13-32. Analysis of Creatine Phosphokinase (U/L) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	112.1	112.6	0.012	0.000 (0.020)	0.994
Medium	141	108.1	108.3			
High	140	115.7	114.9			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of creatine phosphokinase versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	137.7	0.127	-0.002 (0.023)	0.931
Medium	140	132.5			
High	138	139.1			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of creatine phosphokinase versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	106.3	106.1		
Background RH	348	103.0	106.0	-0.1	0.964
Low RH	208	111.5	110.4	4.3	0.382
High RH	211	112.3	109.3	3.2	0.514
Low plus High RH	419	111.9	109.8	3.7	0.315

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-32. Analysis of Creatine Phosphokinase (U/L) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	139.8		
Background RH	346	141.4	1.6	0.733
Low RH	207	141.5	1.7	0.767
High RH	209	145.0	5.2	0.403
Low plus High RH	416	143.3	3.5	0.450

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	99.7	0.006	0.028 (0.013)	0.032*
Medium	256	110.9			
High	255	113.3			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of creatine phosphokinase versus log_2 (1987 dioxin).

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	127.9	0.122	0.007 (0.015)	0.654
Medium	255	133.9			
High	252	133.5			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of creatine phosphokinase versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.23   Creatine Phosphokinase (Discrete)

No significant association between creatine phosphokinase in its discrete form and either group or dioxin was revealed in any of the unadjusted or adjusted Model 1 through 4 analyses (Table 13-33(a-h): p>0.10 for each analysis).

Table 13-33. Analysis of Creatine Phosphokinase (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*68 (8.9)*	*0.81 (0.59,1.10)*	*0.173*
	Comparison	*1,154*	*124 (10.7)*		
Officer	Ranch Hand	305	24 (7.9)	0.95 (0.56,1.61)	0.839
	Comparison	459	38 (8.3)		
Enlisted Flyer	Ranch Hand	133	12 (9.0)	0.68 (0.33,1.42)	0.307
	Comparison	181	23 (12.7)		
Enlisted Groundcrew	Ranch Hand	330	32 (9.7)	0.77 (0.49,1.21)	0.252
	Comparison	514	63 (12.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.82 (0.60,1.14)*	*0.242*
Officer	763	0.92 (0.54,1.59)	0.776
Enlisted Flyer	311	0.70 (0.32,1.53)	0.375
Enlisted Groundcrew	838	0.80 (0.50,1.29)	0.365

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	11 (8.0)	0.94 (0.72,1.22)	0.621
Medium	141	14 (9.9)		
High	140	11 (7.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-33. Analysis of Creatine Phosphokinase (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	0.92 (0.67,1.27)	0.620

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	124 (10.7)		
Background RH	348	32 (9.2)	0.94 (0.62,1.42)	0.772
Low RH	208	18 (8.7)	0.75 (0.44,1.27)	0.282
High RH	211	18 (8.5)	0.70 (0.41,1.18)	0.177
Low plus High RH	419	36 (8.6)	0.72 (0.49,1.07)	0.107

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	1.03 (0.67,1.59)	0.892
Low RH	207	0.67 (0.38,1.16)	0.151
High RH	209	0.76 (0.44,1.31)	0.322
Low plus High RH	416	0.71 (0.47,1.07)	0.105

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-33. Analysis of Creatine Phosphokinase (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) High**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	256	22 (8.6)	0.97 (0.83,1.14)	0.743
Medium	256	23 (9.0)		
High	255	23 (9.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
762	0.90 (0.75,1.09)	0.280

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.24 *Serum Amylase (Continuous)*

No difference between Ranch Hands and Comparisons was seen among all participants in the unadjusted or adjusted Model 1 analysis of serum amylase (Table 13-34(a,b): p>0.26 for each analysis). Stratifying by military occupation in the unadjusted Model 1 analysis did not reveal any group differences (Table 13-34(a): p>0.05 for each analysis). After stratifying by military occupation in the adjusted Model 1 analysis, a significant difference between Ranch Hand and Comparison officers was revealed (Table 13-34(b): difference of adjusted mean=-3.25 U/L, p=0.049). Ranch Hand officers had an adjusted mean serum amylase value of 57.85 U/L versus 61.10 U/L for Comparison officers.

The unadjusted Model 2 analysis of serum amylase was nonsignificant (Table 13-34(c): p=0.080). After adjusting for covariates, a significant inverse association was revealed between initial dioxin and serum amylase in its continuous form (Table 13-34(d): Adjusted Slope=-0.036, p=0.031). The adjusted mean serum amylase values for Ranch Hands in the low, medium, and high dioxin categories were 63.07 U/L, 57.35 U/L, and 57.06 U/L, respectively.

The unadjusted and adjusted Model 3 analyses of serum amylase were nonsignificant (Table 13-34(e,f): p>0.05 for each analysis). A significant inverse relation was seen between 1987 dioxin and serum amylase in both the unadjusted and adjusted Model 4 analysis (Table 13-34(g,h): Slope=-0.019, p=0.029, and Adjusted Slope=-0.020, p=0.048, respectively). The mean serum amylase level was 63.87 U/l for Ranch Hands in the low dioxin category, compared to 62.03 U/l for the medium dioxin category and 58.26 U/l for the high dioxin category.

Table 13-34. Analysis of Serum Amylase (U/L) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*54.37*	*-1.11*	*0.263*
	Comparison	*1,154*	*55.48*		
Officer	Ranch Hand	305	52.92	-2.99	0.056
	Comparison	459	55.90		
Enlisted Flyer	Ranch Hand	133	54.07	-1.69	0.489
	Comparison	181	55.76		
Enlisted Groundcrew	Ranch Hand	330	55.86	0.86	0.571
	Comparison	514	55.00		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*60.07*	*-1.12*	*0.296*
	Comparison	*1,149*	*61.19*		
Officer	Ranch Hand	304	57.85	-3.25	0.049*
	Comparison	459	61.10		
Enlisted Flyer	Ranch Hand	132	59.47	-2.19	0.404
	Comparison	179	61.66		
Enlisted Groundcrew	Ranch Hand	327	62.66	1.36	0.413
	Comparison	511	61.30		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 <$ p-value ≤ 0.050).

Table 13-34. Analysis of Serum Amylase (U/L) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

	Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	**n**	**Unadjusted Mean[a]**	**Adjusted Mean[a,b]**	**R^2**	**Slope (Standard Error)[b,c]**	**p-Value**
Low	138	56.59	56.29	0.039	-0.025 (0.015)	0.080
Medium	141	51.85	51.74			
High	140	52.26	52.65			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of serum amylase versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Initial Dioxin Category Summary Statistics		Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	138	63.07	0.117	-0.036 (0.017)	0.031*
Medium	140	57.35			
High	138	57.06			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of serum amylase versus log$_2$ (initial dioxin).

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	55.48	55.54		
Background RH	348	55.37	54.26	-1.28	0.322
Low RH	208	55.56	55.96	0.42	0.794
High RH	211	51.56	52.59	-2.95	0.057
Low plus High RH	419	53.51	54.24	-1.30	0.277

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-34. Analysis of Serum Amylase (U/L) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	61.20		
Background RH	346	60.00	-1.20	0.404
Low RH	207	61.16	-0.04	0.984
High RH	209	58.76	-2.44	0.166
Low plus High RH	416	59.94	-1.26	0.344

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	56.24	0.006	-0.019 (0.009)	0.029*
Medium	256	54.71			
High	255	52.15			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of serum amylase versus log$_2$ (1987 dioxin).

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

Table 13-34. Analysis of Serum Amylase (U/L) (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	255	63.87	0.071	-0.020 (0.010)	0.048*
Medium	255	62.03			
High	252	58.26			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of serum amylase versus log$_2$ (1987 dioxin).

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.25 Serum Amylase (Discrete)

No significant group difference for all participants was seen in the unadjusted and adjusted Model 1 analyses of serum amylase in its discrete form (Table 13-35(a,b): p>0.37 for each analysis). After stratifying by military occupation, however, a significant difference was seen between Ranch Hands and Comparisons among officers in both the unadjusted and adjusted Model 1 analyses (Table 13-35(a,b): Unadjusted RR=0.28, p=0.042; Adjusted RR=0.27, p=0.038, respectively). Ranch Hand officers had a lower percentage of abnormally high serum amylase values than did Comparison officers (1.0% for Ranch Hand officers and 3.5% for Comparison officers).

All unadjusted and adjusted Model 2, 3, and 4 analyses of serum amylase in its discrete form were nonsignificant (Table 13-35(c-h): p>0.18 for each analysis).

Table 13-35. Analysis of Serum Amylase (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*22 (2.9)*	*0.87 (0.51,1.48)*	*0.595*
	Comparison	*1,154*	*38 (3.3)*		
Officer	Ranch Hand	305	3 (1.0)	0.28 (0.08,0.95)	0.042*
	Comparison	459	16 (3.5)		
Enlisted Flyer	Ranch Hand	133	5 (3.8)	1.14 (0.34,3.82)	0.832
	Comparison	181	6 (3.3)		
Enlisted Groundcrew	Ranch Hand	330	14 (4.2)	1.38 (0.66,2.86)	0.389
	Comparison	514	16 (3.1)		

*: Statistically significant (0.010<p-value≤0.050).

Table 13-35. Analysis of Serum Amylase (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.78 (0.45,1.36)*	*0.378*
Officer	763	0.27 (0.08,0.93)	0.038*
Enlisted Flyer	311	1.00 (0.29,3.41)	0.999
Enlisted Groundcrew	838	1.25 (0.59,2.66)	0.566

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	5 (3.6)	0.83 (0.53,1.30)	0.414
Medium	141	6 (4.3)		
High	140	3 (2.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	0.70 (0.42,1.20)	0.181

[a]Relative risk for a twofold increase in initial dioxin.

Table 13-35. Analysis of Serum Amylase (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	38 (3.3)		
Background RH	348	8 (2.3)	0.61 (0.28,1.33)	0.217
Low RH	208	8 (3.8)	1.21 (0.55,2.63)	0.638
High RH	211	6 (2.8)	0.96 (0.40,2.30)	0.920
Low plus High RH	419	14 (3.3)	1.07 (0.57,2.02)	0.827

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	0.61 (0.28,1.34)	0.216
Low RH	207	0.93 (0.40,2.16)	0.872
High RH	209	0.92 (0.37,2.27)	0.848
Low plus High RH	416	0.92 (0.48,1.79)	0.815

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	7 (2.7)	0.96 (0.73,1.25)	0.755
Medium	256	7 (2.7)		
High	255	8 (3.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 13-35. Analysis of Serum Amylase (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
762	0.88 (0.66,1.19)	0.404

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.26 Antibodies for Hepatitis A

No significant association was seen between either group or dioxin and the existence of antibodies for hepatitis A in the unadjusted and adjusted Model 1 through 4 analyses (Table 13-36(a-h): p>0.07 for each analysis).

Table 13-36. Analysis of Antibodies for Hepatitis A

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*774*	*247 (31.9)*	*0.87 (0.72,1.05)*	*0.153*
	Comparison	*1,173*	*411 (35.0)*		
Officer	Ranch Hand	304	80 (26.3)	0.87 (0.63,1.21)	0.417
	Comparison	462	134 (29.0)		
Enlisted Flyer	Ranch Hand	133	63 (47.4)	1.08 (0.69,1.69)	0.729
	Comparison	185	84 (45.4)		
Enlisted Groundcrew	Ranch Hand	337	104 (30.9)	0.77 (0.58,1.03)	0.079
	Comparison	526	193 (36.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,937*	*0.86 (0.70,1.05)*	*0.136*
Officer	765	0.83 (0.59,1.16)	0.267
Enlisted Flyer	315	1.04 (0.65,1.66)	0.871
Enlisted Groundcrew	857	0.81 (0.60,1.10)	0.185

Table 13-36. Analysis of Antibodies for Hepatitis A (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	49 (35.3)	1.03 (0.88,1.20)	0.731
Medium	143	43 (30.1)		
High	141	50 (35.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
420	1.05 (0.87,1.27)	0.582

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,173	411 (35.0)		
Background RH	350	104 (29.7)	0.79 (0.61,1.03)	0.077
Low RH	210	70 (33.3)	0.92 (0.68,1.26)	0.622
High RH	213	72 (33.8)	0.94 (0.69,1.28)	0.693
Low plus High RH	423	142 (33.6)	0.93 (0.74,1.18)	0.559

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-36. Analysis of Antibodies for Hepatitis A (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	348	0.84 (0.64,1.11)	0.224
Low RH	209	0.80 (0.58,1.12)	0.192
High RH	211	0.93 (0.66,1.30)	0.668
Low plus High RH	420	0.86 (0.67,1.11)	0.254

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	258	74 (28.7)	1.07 (0.98,1.18)	0.137
Medium	257	89 (34.6)		
High	258	83 (32.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	1.06 (0.94,1.19)	0.354

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.27 Serological Evidence of Prior Hepatitis B Infection

Significant overall group differences were revealed in each of the unadjusted and adjusted Model 1 analyses of serological evidence of prior hepatitis B infection (Table 13-37(a,b): Unadjusted RR=0.56, p<0.001; Adjusted RR=0.53, p<0.001, respectively). Comparisons had a higher percentage of prior hepatitis B infections than Ranch Hands (11.0% versus 6.4%, respectively).

After stratifying by military occupation, significant differences between Ranch Hands and Comparisons in both the unadjusted and adjusted Model 1 analyses of prior hepatitis B infection were seen among

officers (Table 13-37(a,b): Unadjusted RR=0.41, p=0.039, Adjusted RR=0.40, p=0.034), as well as among enlisted groundcrew (Table 13-37(a,b): Unadjusted RR=0.57, p=0.017, Adjusted RR=0.56, p=0.016). Among officers, 5.4 percent of Comparisons had prior hepatitis B infections versus 2.3 percent of Ranch Hands. Comparison enlisted groundcrew had a greater percentage of prior hepatitis B infections than Ranch Hand enlisted groundcrew (13.7% versus 8.3%, respectively).

No significant associations were seen between initial dioxin and prior hepatitis B infection in the unadjusted and adjusted Model 2 analyses (Table 13-37(c,d): p>0.19 for each analysis).

The unadjusted Model 3 analysis revealed a significant difference between Ranch Hands in the background dioxin category and Comparisons (Table 13-37(e): Unadjusted RR=0.38, p<0.001). After adjusting for covariates, three contrasts were significant: Ranch Hands in the background dioxin category versus Comparisons (Table 13-37(f): Adjusted RR=0.44, p=0.004), Ranch Hands in the low dioxin category versus Comparisons (Table 13-37(f): Adjusted RR=0.56, p=0.045), and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 13-37(f): Adjusted RR=0.59, p=0.012). The percentages of prior hepatitis B infections for Ranch Hands in the background dioxin category, low dioxin category, and low and high dioxin categories combined were 4.3, 7.1, and 8.3, respectively, versus 11.0 percent for Comparisons.

A significant positive relation between 1987 dioxin and prior hepatitis B infections was seen in the unadjusted Model 4 analysis (Table 13-37(g): Unadjusted RR=1.26, p=0.008). After adjusting for covariates, however, the results were no longer significant (Table 13-37(h): p=0.184).

Table 13-37. Analysis of Serological Evidence of Prior Hepatitis B Infection

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Yes**	**Unadjusted Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*777*	*50 (6.4)*	*0.56 (0.40,0.78)*	*<0.001***
	Comparison	*1,174*	*129 (11.0)*		
Officer	Ranch Hand	307	7 (2.3)	0.41 (0.17,0.96)	0.039*
	Comparison	462	25 (5.4)		
Enlisted Flyer	Ranch Hand	133	15 (11.3)	0.61 (0.31,1.17)	0.138
	Comparison	185	32 (17.3)		
Enlisted Groundcrew	Ranch Hand	337	28 (8.3)	0.57 (0.36,0.91)	0.017*
	Comparison	527	72 (13.7)		

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,941*	*0.53 (0.38,0.76)*	*<0.001***
Officer	768	0.40 (0.17,0.93)	0.034*
Enlisted Flyer	315	0.59 (0.30,1.15)	0.123
Enlisted Groundcrew	858	0.56 (0.35,0.90)	0.016*

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	9 (6.4)	1.18 (0.92,1.51)	0.199
Medium	143	11 (7.7)		
High	141	15 (10.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
421	1.07 (0.79,1.44)	0.666

[a]Relative risk for a twofold increase in initial dioxin.

Table 13-37. Analysis of Serological Evidence of Prior Hepatitis B Infection (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	129 (11.0)		
Background RH	352	15 (4.3)	0.38 (0.22,0.65)	<0.001**
Low RH	211	15 (7.1)	0.61 (0.35,1.06)	0.082
High RH	213	20 (9.4)	0.81 (0.49,1.33)	0.394
Low plus High RH	424	35 (8.3)	0.70 (0.47,1.04)	0.079

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,169		
Background RH	350	0.44 (0.25,0.77)	0.004**
Low RH	210	0.56 (0.31,0.99)	0.045*
High RH	211	0.63 (0.38,1.06)	0.082
Low plus High RH	421	0.59 (0.40,0.89)	0.012*

[a]Relative risk and confidence interval relative to Comparisons.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-37. *Analysis of Serological Evidence of Prior Hepatitis B Infection (Continued)*

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	9 (3.5)	1.26 (1.06,1.50)	0.008**
Medium	258	15 (5.8)		
High	258	26 (10.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
771	1.15 (0.94,1.40)	0.184

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.28   *Antibodies for Hepatitis C*

Both the unadjusted and adjusted Model 1 analyses of hepatitis C antibodies revealed significant overall group differences (Table 13-38(a,b): Unadjusted RR=0.39, p=0.046; Adjusted RR=0.37, p=0.037). A greater percentage of Comparisons had antibodies for hepatitis C than Ranch Hands (1.6% for Comparisons versus 0.6% for Ranch Hands). Stratifying the unadjusted and adjusted Model 1 analyses by military occupation did not reveal any significant results (Table 13-38(a,b): p≥0.17 for each stratum).

All unadjusted and adjusted Model 2, 3, and 4 analyses of hepatitis C antibodies were nonsignificant (Table 13-38(c-h): p>0.05 for each analysis).

Table 13-38. Analysis of Antibodies for Hepatitis C

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*5 (0.6)*	*0.39 (0.15,1.06)*	*0.046**
	Comparison	*1,174*	*19 (1.6)*		
Officer	Ranch Hand	307	1 (0.3)	0.75 (0.07,8.33)	0.816
	Comparison	462	2 (0.4)		
Enlisted Flyer	Ranch Hand	133	0 (0.0)	--	0.232[a]
	Comparison	185	4 (2.2)		
Enlisted Groundcrew	Ranch Hand	337	4 (1.2)	0.47 (0.15,1.47)	0.196
	Comparison	527	13 (2.5)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with antibodies for hepatitis C.

*: Statistically significant (0.010<p-value≤0.050).

--: Results were not presented because of the sparse number of participants with antibodies for hepatitis C.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,941*	*0.37 (0.13,1.02)*	*0.037**
Officer	768	0.74 (0.07,8.20)	0.805
Enlisted Flyer	315	--	--
Enlisted Groundcrew	858	0.45 (0.14,1.41)	0.170

*: Statistically significant (0.010<p-value≤0.050).

--: Results were not presented because of the sparse number of participants with antibodies for hepatitis C.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	1 (0.7)	0.43 (0.08,2.25)	0.237
Medium	143	1 (0.7)		
High	141	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-38. Analysis of Antibodies for Hepatitis C (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
421	0.23 (0.03,1.94)	0.078

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, cumulative degreasing chemical exposure, cumulative industrial chemical exposure, and current alcohol use because of the sparse number of Ranch Hands with antibodies for hepatitis C.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	19 (1.6)		
Background RH	352	3 (0.9)	0.49 (0.14,1.68)	0.257
Low RH	211	1 (0.5)	0.29 (0.04,2.21)	0.234
High RH	213	1 (0.5)	0.30 (0.04,2.28)	0.246
Low plus High RH	424	2 (0.5)	0.30 (0.07,1.29)	0.105

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,169		
Background RH	350	0.62 (0.17,2.19)	0.454
Low RH	210	0.24 (0.03,1.93)	0.180
High RH	211	0.24 (0.03,1.82)	0.166
Low plus High RH	421	0.24 (0.05,1.06)	0.059

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-38. Analysis of Antibodies for Hepatitis C (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	3 (1.2)	0.65 (0.37,1.15)	0.138
Medium	258	1 (0.4)		
High	258	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
771	0.62 (0.36,1.09)	0.099

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for military occupation because of the sparse number of Ranch Hands with antibodies for hepatitis C.

13.2.2.3.29   *Stool Hemoccult*

No overall group differences were seen between Ranch Hands and Comparisons in the unadjusted and adjusted Model 1 analyses of stool hemoccult (Table 13-39(a,b): p>0.54 for each analysis). After stratifying by occupation, a significant group difference was seen among officers in both the unadjusted and adjusted analyses (Table 13-39(a,b): Unadjusted RR=9.12, p=0.041; Adjusted RR=8.99, p=0.043). Officers in the Ranch Hand group had a higher percentage of positive stool hemoccult results than did officers in the Comparison group (2.1% versus 0.2%).

The unadjusted and adjusted Model 2 through 4 analyses did no show any significant associations between dioxin and stool hemoccult (Table 13-39(c-h): p>0.30 for each analysis).

Table 13-39. Analysis of Stool Hemoccult

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*722*	*12 (1.7)*	*1.20 (0.56,2.57)*	*0.645*
	Comparison	*1,078*	*15 (1.4)*		
Officer	Ranch Hand	287	6 (2.1)	9.12 (1.09,76.14)	0.041*
	Comparison	428	1 (0.2)		
Enlisted Flyer	Ranch Hand	125	3 (2.4)	2.08 (0.34,12.62)	0.427
	Comparison	171	2 (1.2)		
Enlisted Groundcrew	Ranch Hand	310	3 (1.0)	0.38 (0.11,1.36)	0.137
	Comparison	479	12 (2.5)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,790*	*1.27 (0.58,2.78)*	*0.545*
Officer	714	8.99 (1.07,75.33)	0.043*
Enlisted Flyer	293	2.00 (0.33,12.26)	0.454
Enlisted Groundcrew	783	0.42 (0.12,1.51)	0.184

*: Statistically significant (0.010<p-value≤0.050).

Note: Results were not adjusted for current cigarette smoking because of the sparse number of participants with a positive stool hemoccult.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	130	3 (2.3)	0.91 (0.48,1.73)	0.763
Medium	134	1 (0.7)		
High	130	2 (1.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-39. Analysis of Stool Hemoccult (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

| | Analysis Results for Log_2 (Initial Dioxin) | |
| | Adjusted Relative Risk | |
n	(95% C.I.)[a]	p-Value
391	1.04 (0.48,2.24)	0.918

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, cumulative industrial chemical exposure, current cigarette smoking, and compliance to dietary restrictions because of the sparse number of Ranch Hands with a positive stool hemoccult.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,078	15 (1.4)		
Background RH	327	6 (1.8)	1.33 (0.51,3.48)	0.561
Low RH	195	3 (1.5)	1.11 (0.32,3.86)	0.875
High RH	199	3 (1.5)	1.08 (0.31,3.78)	0.904
Low plus High RH	394	6 (1.5)	1.09 (0.42,2.85)	0.856

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,073		
Background RH	325	1.68 (0.62,4.58)	0.309
Low RH	194	1.03 (0.29,3.69)	0.958
High RH	197	0.90 (0.25,3.28)	0.872
Low plus High RH	391	0.96 (0.36,2.57)	0.942

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Note: Results were not adjusted for current cigarette smoking because of the sparse number of participants with a positive stool hemoccult.

Table 13-39. Analysis of Stool Hemoccult (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	240	4 (1.7)	1.01 (0.71,1.45)	0.947
Medium	241	5 (2.1)		
High	240	3 (1.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
716	1.26 (0.78,2.04)	0.328

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race and current cigarette smoking because of the sparse number of Ranch Hands with a positive stool hemoccult.

13.2.2.3.30 Protein Profile: Prealbumin (Continuous)

No significant group differences were revealed in the unadjusted and adjusted Model 1 analyses of prealbumin in its continuous form (Table 13-40(a,b): p>0.21 for each analysis).

As initial dioxin increased, a significant decrease in prealbumin was observed in the unadjusted Model 2 analysis (Table 13-40(c): Slope=-0.043, p=0.042). After covariate adjustment, however, the results were no longer significant (Table 13-40(d): p=0.055).

All unadjusted and adjusted Model 3 and 4 analyses of prealbumin in its continuous form were nonsignificant (Table 13-40(e-h): p>0.12 for each analysis).

Table 13-40. Analysis of Protein Profile: Prealbumin (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*28.99*	*0.19*	*0.488*
	Comparison	*1,154*	*28.80*		
Officer	Ranch Hand	305	29.05	0.12	0.771
	Comparison	459	28.92		
Enlisted Flyer	Ranch Hand	133	28.94	0.64	0.326
	Comparison	181	28.30		
Enlisted Groundcrew	Ranch Hand	330	28.95	0.08	0.844
	Comparison	514	28.87		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*29.01*	*0.24*	*0.355*
	Comparison	*1,149*	*28.76*		
Officer	Ranch Hand	304	29.22	0.22	0.599
	Comparison	459	29.00		
Enlisted Flyer	Ranch Hand	132	29.41	0.81	0.211
	Comparison	179	28.60		
Enlisted Groundcrew	Ranch Hand	327	28.60	0.05	0.898
	Comparison	511	28.55		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

		Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	29.93	29.83	0.059	-0.043 (0.021)	0.042*
Medium	141	28.35	28.31			
High	140	28.58	28.73			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of prealbumin versus log_2 (initial dioxin).

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

		Initial Dioxin Category Summary Statistics	Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	30.27	0.144	-0.046 (0.024)	0.055
Medium	140	28.57			
High	138	28.85			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of prealbumin versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	28.80	28.81		
Background RH	348	29.07	28.85	0.04	0.923
Low RH	208	29.13	29.21	0.40	0.355
High RH	211	28.76	28.98	0.17	0.699
Low plus High RH	419	28.94	29.10	0.29	0.389

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-40. Analysis of Protein Profile: Prealbumin (mg/dL) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	28.77		
Background RH	346	28.89	0.12	0.733
Low RH	207	29.43	0.66	0.127
High RH	209	28.77	0.00	0.997
Low plus High RH	416	29.09	0.32	0.321

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	29.21	0.001	-0.014 (0.013)	0.299
Medium	256	29.22			
High	255	28.59			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of prealbumin versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	29.19	0.084	-0.002 (0.015)	0.886
Medium	255	29.82			
High	252	28.77			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of prealbumin versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.31   Protein Profile: Prealbumin (Discrete)

No significant associations with dioxin were seen in the Model 1 through 4 unadjusted and adjusted analyses of prealbumin in its discrete form (Table 13-41(a-h): p>0.16 for each analysis).

Table 13-41. Analysis of Protein Profile: Prealbumin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*16 (2.1)*	*1.62 (0.79,3.29)*	*0.187*
	Comparison	*1,154*	*15 (1.3)*		
Officer	Ranch Hand	305	7 (2.3)	1.77 (0.59,5.33)	0.307
	Comparison	459	6 (1.3)		
Enlisted Flyer	Ranch Hand	133	1 (0.8)	0.45 (0.05,4.37)	0.491
	Comparison	181	3 (1.7)		
Enlisted Groundcrew	Ranch Hand	330	8 (2.4)	2.10 (0.72,6.12)	0.172
	Comparison	514	6 (1.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*1.61 (0.78,3.32)*	*0.198*
Officer	763	1.77 (0.59,5.36)	0.309
Enlisted Flyer	311	0.39 (0.04,3.82)	0.415
Enlisted Groundcrew	838	2.16 (0.72,6.54)	0.171

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	2 (1.4)	1.17 (0.71,1.91)	0.540
Medium	141	4 (2.8)		
High	140	2 (1.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-41. Analysis of Protein Profile: Prealbumin (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)**[a]	**p-Value**
416	1.09 (0.63,1.88)	0.768

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for military occupation because of the sparse number of Ranch Hands with an abnormally low prealbumin level.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	15 (1.3)		
Background RH	348	8 (2.3)	1.67 (0.70,3.99)	0.251
Low RH	208	5 (2.4)	1.90 (0.68,5.30)	0.218
High RH	211	3 (1.4)	1.16 (0.33,4.07)	0.812
Low plus High RH	419	8 (1.9)	1.49 (0.61,3.61)	0.382

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	1.66 (0.68,4.08)	0.268
Low RH	207	2.11 (0.74,6.02)	0.164
High RH	209	1.10 (0.30,4.08)	0.881
Low plus High RH	416	1.52 (0.61,3.80)	0.366

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-41. Analysis of Protein Profile: Prealbumin (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	7 (2.7)	0.97 (0.71,1.32)	0.834
Medium	256	3 (1.2)		
High	255	6 (2.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
762	0.99 (0.68,1.43)	0.942

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.32   Protein Profile: Albumin (Continuous)

All unadjusted and adjusted Model 1 through 4 analyses of albumin in its continuous form were nonsignificant (Table 13-42(a-h): p>0.09 for each analysis).

Table 13-42. Analysis of Protein Profile: Albumin (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*4,187.9*	*0.9* (-24.3,26.1)	*0.945*
	Comparison	*1,154*	*4,187.0*		
Officer	Ranch Hand	305	4,161.3	-13.2 (-53.1,26.7)	0.517
	Comparison	459	4,174.5		
Enlisted Flyer	Ranch Hand	133	4,210.5	14.9 (-46.7,76.6)	0.635
	Comparison	181	4,195.6		
Enlisted Groundcrew	Ranch Hand	330	4,203.3	8.2 (-29.9,46.3)	0.673
	Comparison	514	4,195.1		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*763*	*4,142.1*	*3.2 (-21.6,28.1)*	*0.799*
	Comparison	*1,149*	*4,138.8*		
Officer	Ranch Hand	304	4,106.6	-9.2 (-48.4,30.1)	0.648
	Comparison	459	4,115.8		
Enlisted Flyer	Ranch Hand	132	4,176.7	19.4 (-41.7,80.6)	0.534
	Comparison	179	4,157.2		
Enlisted Groundcrew	Ranch Hand	327	4,148.8	8.6 (-29.1,46.3)	0.655
	Comparison	511	4,140.2		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for $\log_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	138	4,234.1	4,231.1	0.025	-9.287 (9.466)	0.327
Medium	141	4,158.9	4,157.7			
High	140	4,193.6	4,197.6			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	138	4,166.3	0.081	-18.523 (11.081)	0.095
Medium	140	4,074.9			
High	138	4,096.2			

Table 13-42. Analysis of Protein Profile: Albumin (mg/dL) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,154	4,187.0	4,187.4		
Background RH	348	4,179.9	4,172.6	-14.8 (-47.9,18.4)	0.383
Low RH	208	4,196.2	4,198.8	11.4 (-29.2,51.9)	0.583
High RH	211	4,194.3	4,201.4	14.0 (-26.5,54.4)	0.499
Low plus High RH	419	4,195.2	4,200.1	12.7 (-18.1,43.5)	0.420

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,149	4,138.1		
Background RH	346	4,133.5	-4.6 (-38.0,28.7)	0.786
Low RH	207	4,165.0	26.9 (-13.6,67.4)	0.193
High RH	209	4,131.3	-6.8 (-48.3,34.7)	0.748
Low plus High RH	416	4,148.1	10.0 (-21.0,40.9)	0.528

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean	R^2	Slope (Standard Error)	p-Value
Low	256	4,182.8	<0.001	2.239 (6.214)	0.719
Medium	256	4,200.0			
High	255	4,182.0			

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	255	4,146.3	0.054	-5.001 (7.248)	0.490
Medium	255	4,170.9			
High	252	4,111.5			

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.33   Protein Profile: Albumin (Discrete)

Due to a sparse number of participants with an abnormally low albumin level, the analysis was limited in some of the models.

The unadjusted and adjusted Model 1 analyses of albumin in its discrete form showed no significant group differences (Table 13-43(a,b): p>0.37 for each analysis). The Model 2 analysis was not performed since there were no abnormally low albumin values.

Due to a sparse number of abnormalities in the Model 3 analysis, relative risks were only calculated for Ranch Hands in the background dioxin category versus Comparisons. The results of both the unadjusted and adjusted analyses were nonsignificant (Table 13-43(e,f): p>0.09 for each contrast).

A significant inverse association between 1987 dioxin and albumin in its discrete form was seen in each of the unadjusted and adjusted Model 4 analyses (Table 13-43(g,h): Unadjusted RR=0.50, p=0.015; Adjusted RR=0.37, p=0.030). The percentages of participants with abnormally low albumin values in the low, medium, and high 1987 dioxin categories were 1.6, 0.4, and 0.0, respectively.

Table 13-43. Analysis of Protein Profile: Albumin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*5 (0.7)*	*1.25 (0.38,4.12)*	*0.711*
	Comparison	*1,154*	*6 (0.5)*		
Officer	Ranch Hand	305	3 (1.0)	2.27 (0.38,13.67)	0.371
	Comparison	459	2 (0.4)		
Enlisted Flyer	Ranch Hand	133	1 (0.8)	1.36 (0.08,22.00)	0.827
	Comparison	181	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	330	1 (0.3)	0.52 (0.05,5.00)	0.569
	Comparison	514	3 (0.6)		

Table 13-43. Analysis of Protein Profile: Albumin (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*1.23 (0.36,4.20)*	*0.736*
Officer	763	2.26 (0.36,14.04)	0.381
Enlisted Flyer	311	1.75 (0.09,34.58)	0.712
Enlisted Groundcrew	838	0.44 (0.04,4.55)	0.495

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)	p-Value
Low	138	0 (0.0)	--	--
Medium	141	0 (0.0)		
High	140	0 (0.0)		

--: Analysis was not performed because there were no abnormally low albumin values for Ranch Hands with an extrapolated initial dioxin level.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
416	--	--

--: Analysis was not performed because there were no abnormally low albumin values for Ranch Hands with an extrapolated initial dioxin level.

Table 13-43. Analysis of Protein Profile: Albumin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	6 (0.5)		
Background RH	348	5 (1.4)	2.82 (0.84,9.46)	0.093
Low RH	208	0 (0.0)	--	0.636[c]
High RH	211	0 (0.0)	--	0.629[c]
Low plus High RH	419	0 (0.0)	--	0.310[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of
 participants with an abnormally low albumin level.

--: Results were not presented because of the sparse number of participants with an abnormally low albumin level.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	3.06 (0.80,11.70)	0.103
Low RH	207	--	--
High RH	209	--	--
Low plus High RH	416	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with an abnormally low albumin level.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-43. Analysis of Protein Profile: Albumin (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	4 (1.6)	0.50 (0.29,0.86)	0.015*
Medium	256	1 (0.4)		
High	255	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
762	0.37 (0.15,0.94)	0.030*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Results were not adjusted for race and current cigarette smoking because of the sparse number of Ranch Hands with an abnormally low albumin level.

13.2.2.3.34   Protein Profile: α-1-Acid Glycoprotein (Continuous)

No significant group differences were seen in the unadjusted and adjusted Model 1 analyses of α-1-acid glycoprotein in its continuous form (Table 13-44(a,b): p>0.19 for each analysis). The results of the unadjusted Model 2 analysis were nonsignificant (Table 13-44(c): p=0.145). After adjusting for covariates, however, a significant inverse association between initial dioxin and α-1-acid glycoprotein was revealed (Table 13-44(d): Adjusted Slope=-0.038, p<0.001). The adjusted mean α-1-acid glycoprotein values for Ranch Hands in the low, medium, and high initial dioxin categories were 76.97 mg/dL, 76.46 mg/dL, and 71.12 mg/dL, respectively.

All unadjusted and adjusted Model 3 and 4 analyses of α-1-acid glycoprotein were nonsignificant (Table 13-44(e-h): p>0.05 for each analysis).

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Table 13-44. Analysis of Protein Profile: α-1-Acid Glycoprotein (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*78.51*	*0.42*	*0.632*
	Comparison	*1,154*	*78.09*		
Officer	Ranch Hand	305	74.83	-1.14	0.395
	Comparison	459	75.96		
Enlisted Flyer	Ranch Hand	133	80.37	0.92	0.673
	Comparison	181	79.45		
Enlisted Groundcrew	Ranch Hand	330	81.31	1.75	0.198
	Comparison	514	79.56		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*77.53*	*0.16*	*0.849*
	Comparison	*1,149*	*77.37*		
Officer	Ranch Hand	304	74.28	-1.13	0.388
	Comparison	459	75.41		
Enlisted Flyer	Ranch Hand	132	78.53	0.51	0.810
	Comparison	179	78.02		
Enlisted Groundcrew	Ranch Hand	327	80.03	1.30	0.330
	Comparison	511	78.73		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	79.15	79.25	0.009	-0.013 (0.009)	0.145
Medium	141	82.72	82.76			
High	140	78.20	78.07			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of α-1-acid glycoprotein versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	76.97	0.150	-0.038 (0.010)	<0.001**
Medium	140	76.46			
High	138	71.12			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of α-1-acid glycoprotein versus log$_2$ (initial dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	78.09	78.09		
Background RH	348	76.62	76.62	-1.47	0.200
Low RH	208	80.71	80.71	2.62	0.069
High RH	211	79.33	79.33	1.24	0.384
Low plus High RH	419	80.01	80.01	1.92	0.078

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	77.30		
Background RH	346	76.76	-0.54	0.634
Low RH	207	79.45	2.15	0.128
High RH	209	76.44	-0.86	0.544
Low plus High RH	416	77.92	0.62	0.561

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	76.74	0.002	0.006 (0.005)	0.245
Medium	256	78.18			
High	255	80.50			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of α-1-acid glycoprotein versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	77.91	0.080	-0.012 (0.006)	0.054
Medium	255	77.46			
High	252	76.16			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of α-1-acid glycoprotein versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.35   Protein Profile: α-1-Acid Glycoprotein (Discrete)

The unadjusted and adjusted Model 1, 2, and 4 analyses of α-1-acid glycoprotein in its discrete form were nonsignificant (Table 13-45(a-d,g,h): p>0.10 for each analysis).

A significant difference between Ranch Hands in the low dioxin category and Comparisons was revealed in the unadjusted Model 3 analysis (Table 13-45(e): Unadjusted RR=1.79, p=0.044). After covariate adjustment, however, the results were no longer significant (Table 13-45(f): p=0.051).

Table 13-45. Analysis of Protein Profile: α-1-Acid Glycoprotein (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*46 (6.0)*	*1.27 (0.85,1.90)*	*0.242*
	Comparison	*1,154*	*55 (4.8)*		
Officer	Ranch Hand	305	11 (3.6)	0.82 (0.39,1.74)	0.607
	Comparison	459	20 (4.4)		
Enlisted Flyer	Ranch Hand	133	11 (8.3)	2.24 (0.84,5.94)	0.105
	Comparison	181	7 (3.9)		
Enlisted Groundcrew	Ranch Hand	330	24 (7.3)	1.36 (0.77,2.39)	0.283
	Comparison	514	28 (5.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*1.23 (0.82,1.86)*	*0.323*
Officer	763	0.82 (0.38,1.73)	0.594
Enlisted Flyer	311	2.20 (0.82,5.93)	0.118
Enlisted Groundcrew	838	1.30 (0.73,2.32)	0.375

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	9 (6.5)	0.89 (0.67,1.20)	0.449
Medium	141	13 (9.2)		
High	140	8 (5.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	0.76 (0.54,1.08)	0.111

[a]Relative risk for a twofold increase in initial dioxin.

Table 13-45. Analysis of Protein Profile: α-1-Acid Glycoprotein (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	55 (4.8)		
Background RH	348	15 (4.3)	0.88 (0.49,1.59)	0.681
Low RH	208	17 (8.2)	1.79 (1.02,3.15)	0.044*
High RH	211	13 (6.2)	1.33 (0.71,2.49)	0.368
Low plus High RH	419	30 (7.2)	1.54 (0.97,2.45)	0.067

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	0.95 (0.52,1.73)	0.856
Low RH	207	1.80 (1.00,3.26)	0.051
High RH	209	1.15 (0.60,2.21)	0.673
Low plus High RH	416	1.44 (0.89,2.32)	0.137

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	12 (4.7)	1.03 (0.86,1.24)	0.732
Medium	256	14 (5.5)		
High	255	19 (7.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 13-45. Analysis of Protein Profile: α-1-Acid Glycoprotein (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
762	0.93 (0.75,1.15)	0.505

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.36 Protein Profile: α-1-Antitrypsin (Continuous)

All unadjusted and adjusted Model 1 and 2 analyses of α-1-antitrypsin in its continuous form showed no significant group differences or associations with initial dioxin (Table 13-46(a-d): p>0.05 for each analysis).

The unadjusted Model 3 analysis revealed a significant difference between Ranch Hands in the low dioxin category and Comparisons, as well as a significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-46(e): difference of means=4.1 mg/dL, p=0.037; difference of means=3.6 mg/dL, p=0.015, respectively). After adjusting for covariates, however, no contrasts were significant (Table 13-46(f): p>0.11 for each contrast).

No significant associations were seen between 1987 dioxin and α-1-antitrypsin in the unadjusted and adjusted Model 4 analyses (Table 13-46(g,h): p≥0.12 for each analysis).

Table 13-46. Analysis of Protein Profile: α-1-Antitrypsin (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*142.1*	*1.9*	*0.119*
	Comparison	*1,154*	*140.2*		
Officer	Ranch Hand	305	137.2	0.6	0.753
	Comparison	459	136.6		
Enlisted Flyer	Ranch Hand	133	147.0	0.4	0.902
	Comparison	181	146.7		
Enlisted Groundcrew	Ranch Hand	330	144.7	3.5	0.056
	Comparison	514	141.1		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Table 13-46. Analysis of Protein Profile: α-1-Antitrypsin (mg/dL) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*140.2*	*1.2*	*0.320*
	Comparison	*1,149*	*139.0*		
Officer	Ranch Hand	304	135.0	0.3	0.867
	Comparison	459	134.7		
Enlisted Flyer	Ranch Hand	132	141.4	-1.2	0.668
	Comparison	179	142.7		
Enlisted Groundcrew	Ranch Hand	327	143.4	2.9	0.107
	Comparison	511	140.6		

[a]Transformed from square root scale.

[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[c]P-value was based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	143.9	143.9	0.001	0.010 (0.039)	0.797
Medium	141	145.2	145.2			
High	140	142.3	142.3			

[a]Transformed from square root scale.

[b]Adjusted for body mass index at the time of the blood measurement of dioxin.

[c]Slope and standard error based on square root of α-1-antitrypsin versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	142.4	0.143	-0.048 (0.043)	0.267
Medium	140	140.7			
High	138	136.5			

[a]Transformed from square root scale.

[b]Slope and standard error based on square root of α-1-antitrypsin versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-46. Analysis of Protein Profile: α-1-Antitrypsin (mg/dL) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	140.2	140.2		
Background RH	348	139.8	139.8	-0.4	0.781
Low RH	208	144.3	144.3	4.1	0.037*
High RH	211	143.3	143.4	3.2	0.106
Low plus High RH	419	143.8	143.8	3.6	0.015*

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	138.9		
Background RH	346	139.3	0.4	0.803
Low RH	207	141.9	3.0	0.114
High RH	209	139.5	0.6	0.734
Low plus High RH	416	140.7	1.8	0.208

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	139.3	0.003	0.037 (0.024)	0.120
Medium	256	143.8			
High	255	142.9			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of α-1-antitrypsin versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	139.9	0.116	-0.001 (0.027)	0.982
Medium	255	142.9			
High	252	138.9			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of α-1-antitrypsin versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.37   *Protein Profile: α-1-Antitrypsin (Discrete)*

No significant associations with dioxin were revealed in the unadjusted and adjusted Model 1, 2, and 4 analyses of α-1-antitrypsin in its discrete form (Table 13-47(a-d,g,h): p>0.12 for each analysis).

Three significant contrasts were revealed in the unadjusted Model 3 analysis of abnormally high α-1-antitrypsin values (Table 13-47(e): Unadjusted RR=1.56, p=0.047 for Ranch Hands in the low dioxin category versus Comparisons; Unadjusted RR=1.56, p=0.047 for Ranch Hands in the high dioxin category versus Comparisons; and Unadjusted RR=1.56, p=0.010 for Ranch Hands in the low and high dioxin categories combined versus Comparisons). The adjusted Model 3 analysis of abnormally high α-1-antitrypsin values revealed a significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 13-47(f): Adjusted RR=1.59, p=0.042), as well as a significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-47(f): Adjusted RR=1.48, p=0.030, respectively). Abnormally high α-1-antitrypsin values were found in 9.9 percent of the Comparisons, 14.4 percent of the Ranch Hands in the low dioxin category, and 14.1 percent of the Ranch Hands in the low and high dioxin categories combined. Unadjusted and adjusted analyses of associations between dioxin category and the percentage of participants with abnormally low α-1-antitrypsin values were nonsignificant (Table 13-47(e,f): p>0.10 for each contrast).

Table 13-47. Analysis of Protein Profile: α-1-Antitrypsin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Abnormal Low	Number (%) Normal	Abnormal High	Abnormal Low vs. Normal Unadjusted Relative Risk (95% C.I.)	p-Value	Abnormal High vs. Normal Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*8 (1.0)*	*672 (87.5)*	*88 (11.5)*	*0.61 (0.27,1.39)*	*0.236*	*1.17 (0.87,1.57)*	*0.292*
	Comparison	*1,154*	*20 (1.7)*	*1,020 (88.4)*	*114 (9.9)*				
Officer	Ranch Hand	305	6 (2.0)	276 (90.5)	23 (7.5)	0.90 (0.32,2.51)	0.844	1.02 (0.59,1.76)	0.952
	Comparison	459	10 (2.2)	415 (90.4)	34 (7.4)				
Enlisted Flyer	Ranch Hand	133	0 (0.0)	111 (83.5)	22 (16.5)	--	0.999[a]	1.35 (0.72,2.55)	0.349
	Comparison	181	1 (0.6)	157 (86.7)	23 (12.7)				
Enlisted Groundcrew	Ranch Hand	330	2 (0.6)	285 (86.4)	43 (13.0)	0.35 (0.07,1.63)	0.180	1.19 (0.78,1.81)	0.429
	Comparison	514	9 (1.8)	448 (87.2)	57 (11.1)				

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with current hepatomegaly.

--: Results were not presented because of the sparse number of participants with an abnormally low α-1-antitrypsin level.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Abnormal Low vs. Normal Adjusted Relative Risk (95% C.I.)	p-Value	Abnormal High vs. Normal Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.61 (0.27,1.40)*	*0.242*	*1.16 (0.86,1.58)*	*0.324*
Officer	763	0.94 (0.34,2.62)	0.902	1.00 (0.57,1.74)	0.992
Enlisted Flyer	311	--	--	1.28 (0.67,2.45)	0.458
Enlisted Groundcrew	838	0.33 (0.07,1.55)	0.160	1.23 (0.79,1.90)	0.361

--: Results were not presented because of the sparse number of participants with an abnormally low α-1-antitrypsin level.

Note: Results were not adjusted for race and current cigarette smoking because of the sparse number of participants with an abnormally low α-1-antitrypsin level.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category		Initial Dioxin Category Summary Statistics Number (%)			Analysis Results for Log_2 (Initial Dioxin)[a]			
					Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]	p-Value
Low	138	1 (0.7)	120 (87.0)	17 (12.3)	0.74 (0.23,2.42)	0.622	0.99 (0.80,1.22)	0.909
Medium	141	0 (0.0)	117 (83.0)	24 (17.0)				
High	140	1 (0.7)	121 (86.4)	18 (12.9)				

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)				
	Abnormal Low vs. Normal		Abnormal High vs. Normal		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value	
416	0.54 (0.14,2.09)	0.374	0.93 (0.74,1.17)	0.527	

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, current cigarette smoking, and current wine consumption because of the sparse number of Ranch Hands with an abnormally low α-1-antitrypsin level.

Table 13-47. Analysis of Protein Profile: α-1-Antitrypsin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	20 (1.7)	1,020 (88.4)	114 (9.9)				
Background RH	348	6 (1.7)	314 (90.2)	28 (8.0)	0.88 (0.35,2.22)	0.783	0.72 (0.47,1.12)	0.145
Low RH	208	1 (0.5)	177 (85.1)	30 (14.4)	0.30 (0.04,2.22)	0.236	1.56 (1.01,2.40)	0.047*
High RH	211	1 (0.5)	181 (85.8)	29 (13.7)	0.31 (0.04,2.33)	0.254	1.56 (1.01,2.43)	0.047*
Low plus High RH	419	2 (0.5)	358 (85.4)	59 (14.1)	0.30 (0.07,1.30)	0.109	1.56 (1.11,2.19)	0.010**

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).   **: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149				
Background RH	346	0.81 (0.32,2.07)	0.659	0.79 (0.51,1.24)	0.308
Low RH	207	0.33 (0.04,2.49)	0.282	1.59 (1.02,2.49)	0.042*
High RH	209	0.35 (0.04,2.77)	0.321	1.37 (0.86,2.18)	0.189
Low plus High RH	416	0.34 (0.08,1.50)	0.154	1.48 (1.04,2.10)	0.030*

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.
    Results were not adjusted for race and current cigarette smoking because of the sparse number of participants with abnormally low α-1-antitrypsin.

Table 13-47. Analysis of Protein Profile: α-1-Antitrypsin (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

| 1987 Dioxin Category | n | 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log$_2$ (1987 Dioxin)[a] | | | |
| | | Number (%) | | | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	5 (2.0)	232 (90.6)	19 (7.4)	0.70 (0.44,1.11)	0.129	1.10 (0.96,1.27)	0.160
Medium	256	2 (0.8)	221 (86.3)	33 (12.9)				
High	255	1 (0.4)	219 (85.9)	35 (13.7)				

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| n | Analysis Results for Log$_2$ (1987 Dioxin) | | | |
| | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
762	0.73 (0.46,1.19)	0.207	1.11 (0.96,1.29)	0.149

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, military occupation, and current cigarette smoking because of the sparse number of Ranch Hands with an abnormally low α-1-antitrypsin level.

13.2.2.3.38   Protein Profile: α-2-Macroglobulin (Continuous)

All unadjusted and adjusted Model 1 through 4 analyses of α-2-macroglobulin in its continuous form were nonsignificant (Table 13-48(a-h): p>0.11 for each analysis).

Table 13-48. Analysis of Protein Profile: α-2-Macroglobulin (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*185.7*	*-0.3*	*0.898*
	Comparison	*1,154*	*186.1*		
Officer	Ranch Hand	305	187.2	3.1	0.458
	Comparison	459	184.1		
Enlisted Flyer	Ranch Hand	133	194.5	-5.5	0.426
	Comparison	181	199.9		
Enlisted Groundcrew	Ranch Hand	330	181.0	-2.2	0.582
	Comparison	514	183.1		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*173.4*	*-1.7*	*0.469*
	Comparison	*1,149*	*175.1*		
Officer	Ranch Hand	304	166.4	1.6	0.649
	Comparison	459	164.9		
Enlisted Flyer	Ranch Hand	132	173.5	-8.3	0.152
	Comparison	179	181.8		
Enlisted Groundcrew	Ranch Hand	327	178.3	-2.4	0.509
	Comparison	511	180.7		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 13-48. Analysis of Protein Profile: α-2-Macroglobulin (mg/dL) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	190.5	191.1	0.018	-0.013 (0.012)	0.267
Medium	141	187.3	187.5			
High	140	181.0	180.2			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of α-2-macroglobulin versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	168.8	0.215	-0.002 (0.013)	0.851
Medium	140	170.3			
High	138	165.1			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of α-2-macroglobulin versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	186.1	185.9		
Background RH	348	184.9	187.2	1.3	0.717
Low RH	208	191.0	190.1	4.2	0.335
High RH	211	181.6	179.4	-6.5	0.119
Low plus High RH	419	186.2	184.7	-1.2	0.687

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-48. Analysis of Protein Profile: α-2-Macroglobulin (mg/dL) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	174.2		
Background RH	346	174.2	0.0	0.986
Low RH	207	176.0	1.8	0.628
High RH	209	168.6	-5.6	0.133
Low plus High RH	416	172.2	-2.0	0.486

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	184.4	0.001	-0.006 (0.007)	0.385
Medium	256	189.8			
High	255	182.8			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of α-2-macroglobulin versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	170.7	0.176	-0.006 (0.007)	0.391
Medium	255	173.4			
High	252	170.7			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of α-2-macroglobulin versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.39   Protein Profile: α-2-Macroglobulin (Discrete)

No significant associations with either group or dioxin were revealed in the unadjusted and adjusted Model 1 through 4 analyses of α-2-macroglobulin in its discrete form (Table 13-49(a-h): p>0.26 for each analysis).

Table 13-49. Analysis of Protein Profile: α-2-Macroglobulin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*105 (13.7)*	*0.96 (0.74,1.25)*	*0.779*
	Comparison	*1,154*	*163 (14.1)*		
Officer	Ranch Hand	305	44 (14.4)	1.19 (0.78,1.82)	0.423
	Comparison	459	57 (12.4)		
Enlisted Flyer	Ranch Hand	133	21 (15.8)	0.87 (0.48,1.59)	0.659
	Comparison	181	32 (17.7)		
Enlisted Groundcrew	Ranch Hand	330	40 (12.1)	0.82 (0.54,1.24)	0.346
	Comparison	514	74 (14.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.90 (0.68,1.19)*	*0.459*
Officer	763	1.16 (0.75,1.81)	0.506
Enlisted Flyer	311	0.73 (0.39,1.37)	0.327
Enlisted Groundcrew	838	0.78 (0.50,1.21)	0.263

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	20 (14.5)	0.92 (0.75,1.13)	0.427
Medium	141	26 (18.4)		
High	140	18 (12.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-49. Analysis of Protein Profile: α-2-Macroglobulin (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.06 (0.82,1.38)	0.638

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	163 (14.1)		
Background RH	348	40 (11.5)	0.93 (0.64,1.36)	0.725
Low RH	208	33 (15.9)	1.08 (0.71,1.65)	0.711
High RH	211	31 (14.7)	0.90 (0.59,1.38)	0.631
Low plus High RH	419	64 (15.3)	0.99 (0.71,1.36)	0.934

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	0.87 (0.58,1.29)	0.484
Low RH	207	0.96 (0.62,1.50)	0.865
High RH	209	0.89 (0.56,1.42)	0.619
Low plus High RH	416	0.92 (0.65,1.30)	0.654

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	26 (10.2)	1.05 (0.92,1.19)	0.457
Medium	256	37 (14.5)		
High	255	41 (16.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
762	1.04 (0.88,1.23)	0.661

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.40 Protein Profile: Apolipoprotein B (Continuous)

The unadjusted and adjusted Model 1 through 4 analyses of apolipoprotein B in its continuous form did not reveal any significant associations with either group or dioxin (Table 13-50(a-h): p>0.07 for each analysis).

Table 13-50. Analysis of Protein Profile: Apolipoprotein B (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*102.1*	*-1.0*	*0.372*
	Comparison	*1,154*	*103.1*		
Officer	Ranch Hand	305	98.0	-1.7	0.314
	Comparison	459	99.8		
Enlisted Flyer	Ranch Hand	133	104.6	-0.2	0.955
	Comparison	181	104.8		
Enlisted Groundcrew	Ranch Hand	330	104.9	-0.6	0.721
	Comparison	514	105.5		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Table 13-50. Analysis of Protein Profile: Apolipoprotein B (mg/dL) (Continuous)
(Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*102.0*	*-0.9*	*0.392*
	Comparison	*1,149*	*103.0*		
Officer	Ranch Hand	304	99.3	-1.3	0.448
	Comparison	459	100.6		
Enlisted Flyer	Ranch Hand	132	104.7	-0.4	0.875
	Comparison	179	105.1		
Enlisted Groundcrew	Ranch Hand	327	102.3	-0.8	0.637
	Comparison	511	103.1		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	99.5	99.3	0.015	0.034 (0.042)	0.419
Medium	141	106.3	106.2			
High	140	103.1	103.4			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of apolipoprotein B versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	99.3	0.051	-0.024 (0.049)	0.628
Medium	140	103.8			
High	138	100.5			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of apolipoprotein B versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	103.1	103.1		
Background RH	348	101.1	100.5	-2.6	0.073
Low RH	208	102.5	102.7	-0.4	0.811
High RH	211	103.5	104.0	0.9	0.616
Low plus High RH	419	103.0	103.4	0.3	0.860

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	103.1		
Background RH	346	102.0	-1.1	0.484
Low RH	207	102.8	-0.3	0.864
High RH	209	101.1	-2.0	0.278
Low plus High RH	416	101.9	-1.2	0.400

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	100.6	0.003	0.038 (0.026)	0.151
Medium	256	102.0			
High	255	103.7			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of apolipoprotein B versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	103.9	0.039	-0.007 (0.031)	0.830
Medium	255	104.7			
High	252	102.7			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of apolipoprotein B versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.41   Protein Profile: Apolipoprotein B (Discrete)

All unadjusted and adjusted Model 1 through 4 analyses of apolipoprotein B in its discrete form showed
no significant associations with either group or dioxin (Table 13-51(a-h): p>0.07 for each analysis).

Table 13-51. Analysis of Protein Profile: Apolipoprotein B (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*9 (1.2)*	*0.51 (0.24,1.10)*	*0.074*
	Comparison	*1,154*	*26 (2.3)*		
Officer	Ranch Hand	305	4 (1.3)	0.60 (0.19,1.92)	0.386
	Comparison	459	10 (2.2)		
Enlisted Flyer	Ranch Hand	133	1 (0.8)	0.27 (0.03,2.31)	0.230
	Comparison	181	5 (2.8)		
Enlisted Groundcrew	Ranch Hand	330	4 (1.2)	0.56 (0.18,1.78)	0.326
	Comparison	514	11 (2.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.52 (0.24,1.13)*	*0.084*
Officer	763	0.62 (0.19,2.00)	0.423
Enlisted Flyer	311	0.27 (0.03,2.36)	0.237
Enlisted Groundcrew	838	0.56 (0.18,1.79)	0.330

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	1 (0.7)	1.03 (0.53,1.99)	0.929
Medium	141	3 (2.1)		
High	140	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.18 (0.50,2.82)	0.707

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with an abnormally high apolipoprotein B level.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	26 (2.3)		
Background RH	348	4 (1.1)	0.49 (0.17,1.41)	0.183
Low RH	208	3 (1.4)	0.64 (0.19,2.14)	0.469
High RH	211	2 (0.9)	0.43 (0.10,1.83)	0.252
Low plus High RH	419	5 (1.2)	0.52 (0.20,1.40)	0.197

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	0.50 (0.17,1.47)	0.207
Low RH	207	0.65 (0.19,2.19)	0.485
High RH	209	0.41 (0.09,1.80)	0.238
Low plus High RH	416	0.51 (0.19,1.40)	0.192

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	3 (1.2)	1.10 (0.74,1.64)	0.651
Medium	256	4 (1.6)		
High	255	2 (0.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
762	1.22 (0.74,2.00)	0.439

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.42   Protein Profile: C3 Complement (Continuous)

No significant associations between either group or dioxin and C3 complement in its continuous form were seen in the unadjusted and adjusted Model 1 and 2 analyses (Table 13-52(a-d): p>0.27 for each analysis).

The unadjusted Model 3 analysis of C3 complement revealed three significant contrasts (Table 13-52(e): difference of means=4.7 mg/dL, p=0.003 for Ranch Hands in the low dioxin category versus Comparisons; difference of means=3.2 mg/dL, p=0.038 for Ranch Hands in the high dioxin category versus Comparisons; difference of means=3.9 mg/dL, p<0.001 for Ranch Hands in the low and high dioxin categories combined versus Comparisons). The adjusted Model 3 analysis of C3 complement revealed a significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 13-52(f): difference of adjusted means=3.8 mg/dL, p=0.011). Ranch Hands in the low dioxin category had a mean C3 complement value of 124.2 mg/dL versus 120.4 mg/dL for Comparisons.

A significant positive relation was seen between 1987 dioxin and C3 complement in the unadjusted Model 4 analysis (Table 13-52(g): Slope=0.126, p<0.001). After covariate adjustment, however, the results were no longer significant (Table 13-52(h): p=0.407).

Table 13-52. Analysis of Protein Profile: C3 Complement (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*119.9*	*0.7*	*0.461*
	Comparison	*1,154*	*119.2*		
Officer	Ranch Hand	305	114.2	1.4	0.355
	Comparison	459	112.8		
Enlisted Flyer	Ranch Hand	133	121.8	-1.1	0.651
	Comparison	181	122.8		
Enlisted Groundcrew	Ranch Hand	330	124.6	0.9	0.565
	Comparison	514	123.7		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*121.2*	*0.8*	*0.404*
	Comparison	*1,149*	*120.5*		
Officer	Ranch Hand	304	116.5	1.3	0.369
	Comparison	459	115.2		
Enlisted Flyer	Ranch Hand	132	122.2	-0.9	0.694
	Comparison	179	123.1		
Enlisted Groundcrew	Ranch Hand	327	124.5	0.9	0.520
	Comparison	511	123.6		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	121.2	121.6	0.045	0.037 (0.033)	0.274
Medium	141	126.8	127.0			
High	140	124.2	123.7			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of C3 complement versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	120.9	0.173	-0.014 (0.037)	0.707
Medium	140	124.2			
High	138	119.8			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of C3 complement versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

*Table 13-52. Analysis of Protein Profile: C3 Complement (mg/dL) (Continuous)
(Continued)*

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	119.2	119.1		
Background RH	348	115.1	116.6	-2.5	0.051
Low RH	208	124.4	123.8	4.7	0.003**
High RH	211	123.8	122.3	3.2	0.038*
Low plus High RH	419	124.1	123.0	3.9	<0.001**

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	120.4		
Background RH	346	120.1	-0.3	0.835
Low RH	207	124.2	3.8	0.011*
High RH	209	119.9	-0.5	0.738
Low plus High RH	416	122.0	1.6	0.154

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	256	114.0	0.045	0.126 (0.021)	<0.001**
Medium	256	120.8			
High	255	125.3			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of C3 complement versus log$_2$ (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	255	121.3	0.204	0.019 (0.023)	0.407
Medium	255	123.6			
High	252	123.9			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of C3 complement versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.43   Protein Profile: C3 Complement (Discrete)

All unadjusted and adjusted Model 1 and 2 analyses of C3 complement in its discrete form were nonsignificant (Table 13-53(a-d): p>0.19 for each analysis).

A significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons was seen in the unadjusted Model 3 analysis of C3 complement (Table 13-53(e): p=0.034). The remaining unadjusted contrasts were nonsignificant (Table 13-53(e): p>0.09 for each contrast). Adjusting for covariates in the Model 3 analysis revealed no significant differences in dioxin category (Table 13-53(f): p>0.54 for each contrast). Adjusted results were not given for the low dioxin category and low and high dioxin categories combined due to a sparse number of abnormalities.

The unadjusted Model 4 analysis revealed a significant relation between 1987 dioxin and C3 complement (Table 13-53(g): Unadjusted RR=0.64, p=0.038). The results were no longer significant, however, after adjusting for covariates (Table 13-53(h): p=0.265).

Table 13-53. Analysis of Protein Profile: C3 Complement (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*10 (1.3)*	*0.71 (0.33,1.52)*	*0.371*
	Comparison	*1,154*	*21 (1.8)*		
Officer	Ranch Hand	305	8 (2.6)	1.00 (0.41,2.48)	0.994
	Comparison	459	12 (2.6)		
Enlisted Flyer	Ranch Hand	133	1 (0.8)	0.27 (0.03,2.31)	0.230
	Comparison	181	5 (2.8)		
Enlisted Groundcrew	Ranch Hand	330	1 (0.3)	0.39 (0.04,3.48)	0.397
	Comparison	514	4 (0.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.68 (0.31,1.48)*	*0.321*
Officer	763	0.99 (0.39,2.47)	0.975
Enlisted Flyer	311	0.23 (0.03,2.13)	0.198
Enlisted Groundcrew	838	0.37 (0.04,3.42)	0.384

Note: Results were not adjusted for race because of the sparse number of participants with an abnormally low C3 complement level.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	0 (0.0)	1.78 (0.49,6.39)	0.394
Medium	141	0 (0.0)		
High	140	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-53. Analysis of Protein Profile: C3 Complement (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
419	2.83 (0.19,42.52)	0.442

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, cumulative degreasing chemical exposure, cumulative industrial chemical exposure, lifetime alcohol history, and current cigarette smoking because of the sparse number of Ranch Hands with an abnormally low C3 complement level.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	21 (1.8)		
Background RH	348	8 (2.3)	1.10 (0.48,2.53)	0.818
Low RH	208	0 (0.0)	--	0.098[c]
High RH	211	1 (0.5)	0.29 (0.04,2.19)	0.231
Low plus High RH	419	1 (0.2)	--	0.034*[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormally low C3 complement level.

*: Statistically significant (0.010<p-value≤0.050).

--: Results were not presented because of the sparse number of participants with an abnormally low C3 complement level.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-53. Analysis of Protein Profile: C3 Complement (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	0.90 (0.38,2.11)	0.805
Low RH	207	--	--
High RH	209	0.53 (0.06,4.29)	0.549
Low plus High RH	416	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with an abnormally low C3 complement level.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race because of the sparse number of participants with an abnormally low C3 complement level.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	5 (2.0)	0.64 (0.41,0.98)	0.038*
Medium	256	3 (1.2)		
High	255	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value$\leq$0.050).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
762	0.76 (0.46,1.24)	0.265

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with an abnormally low C3 complement level.

13.2.2.3.44 Protein Profile: C4 Complement (Continuous)

No overall group differences were seen between Ranch Hands and Comparisons in the unadjusted and adjusted Model 1 analyses of C4 complement in its continuous form (Table 13-54(a,b): p>0.20 for each analysis). Stratifying the unadjusted and adjusted analyses by military occupation revealed a significant difference between Ranch Hands and Comparisons in the officer stratum (Table 13-54(a,b): difference of means=-0.83 mg/dL, p=0.044 for the unadjusted analysis; difference of adjusted means=-0.91 mg/dL, p=0.032 for the adjusted analysis). All remaining occupational strata in the unadjusted and adjusted analyses were nonsignificant (Table 13-54(a,b): p>0.36 for each stratum). Among officers, Ranch Hands had a lower adjusted mean C4 complement value than Comparisons (23.56 mg/dL and 24.46 mg/dL, respectively).

The unadjusted Model 2 analysis of C4 complement in its continuous form was nonsignificant (Table 13-54(c): p=0.230). As initial dioxin increased, however, a significant decrease in C4 complement was observed in the adjusted Model 2 analysis (Table 13-54(d): Adjusted Slope=-0.053, p=0.041). The adjusted mean C4 complement values in the low, medium, and high initial dioxin categories were 23.52 mg/dL, 24.47 mg/dL, and 22.90 mg/dL, respectively.

All unadjusted and adjusted Model 3 and 4 analyses of C4 complement in its continuous form were nonsignificant (Table 13-54(e-h): p>0.08 for each analysis).

Table 13-54. Analysis of Protein Profile: C4 Complement (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*22.41*	*-0.33*	*0.209*
	Comparison	*1,154*	*22.74*		
Officer	Ranch Hand	305	21.44	-0.83	0.044*
	Comparison	459	22.27		
Enlisted Flyer	Ranch Hand	133	22.95	0.53	0.413
	Comparison	181	22.42		
Enlisted Groundcrew	Ranch Hand	330	23.11	-0.18	0.657
	Comparison	514	23.29		

[a]Transformed from square root scale.

[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[c]P-value was based on difference of means on square root scale.

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*24.18*	*-0.31*	*0.248*
	Comparison	*1,149*	*24.49*		
Officer	Ranch Hand	304	23.56	-0.91	0.032*
	Comparison	459	24.46		
Enlisted Flyer	Ranch Hand	132	24.67	0.60	0.367
	Comparison	179	24.07		
Enlisted Groundcrew	Ranch Hand	327	24.65	-0.10	0.807
	Comparison	511	24.75		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	22.37	22.38	0.004	-0.026 (0.022)	0.230
Medium	141	23.58	23.58			
High	140	22.24	22.24			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of C4 complement versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	138	23.52	0.039	-0.053 (0.026)	0.041*
Medium	140	24.47			
High	138	22.90			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of C4 complement versus log_2 (initial dioxin).

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	22.74	22.74		
Background RH	348	22.04	22.14	-0.60	0.088
Low RH	208	23.13	23.09	0.35	0.414
High RH	211	22.35	22.24	-0.50	0.244
Low plus High RH	419	22.73	22.66	-0.08	0.812

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

**Table 13-54. Analysis of Protein Profile: C4 Complement (mg/dL) (Continuous)
(Continued)**

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	24.47		
Background RH	346	24.11	-0.36	0.325
Low RH	207	24.69	0.22	0.611
High RH	209	23.69	-0.78	0.085
Low plus High RH	416	24.19	-0.28	0.408

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	21.74	0.002	0.016 (0.013)	0.227
Medium	256	22.80			
High	255	22.72			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of C4 complement versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	24.21	0.075	-0.014 (0.015)	0.342
Medium	255	24.82			
High	252	24.07			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of C4 complement versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.45   Protein Profile: C4 Complement (Discrete)

No significant associations between dioxin and C4 complement in its discrete form were revealed in the unadjusted and adjusted Model 1, 3, and 4 analyses (Table 13-55(a,b,e-h): p>0.07 for each analysis).

A significant positive association between initial dioxin and C4 complement was shown in each of the unadjusted and adjusted Model 2 analyses (Table 13-55(c,d): Unadjusted RR=1.43, p=0.009; Adjusted RR=1.80, p<0.001). The percentages of participants with abnormally low C4 complement values in the low, medium, and high initial dioxin categories were 5.8, 3.5, and 11.4, respectively.

Table 13-55. Analysis of Protein Profile: C4 Complement (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*57 (7.4)*	*0.94 (0.66,1.32)*	*0.708*
	Comparison	*1,154*	*91 (7.9)*		
Officer	Ranch Hand	305	28 (9.2)	1.19 (0.71,1.99)	0.514
	Comparison	459	36 (7.8)		
Enlisted Flyer	Ranch Hand	133	11 (8.3)	0.77 (0.35,1.68)	0.508
	Comparison	181	19 (10.5)		
Enlisted Groundcrew	Ranch Hand	330	18 (5.5)	0.77 (0.43,1.37)	0.371
	Comparison	514	36 (7.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.93 (0.66,1.32)*	*0.688*
Officer	763	1.20 (0.71,2.01)	0.491
Enlisted Flyer	311	0.75 (0.34,1.65)	0.475
Enlisted Groundcrew	838	0.77 (0.43,1.38)	0.376

(c) MODEL 2: RANCH HANDS − INITIAL DIOXIN − UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	8 (5.8)	1.43 (1.10,1.87)	0.009**
Medium	141	5 (3.5)		
High	140	16 (11.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.80 (1.26,2.57)	<0.001**

[a]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	91 (7.9)		
Background RH	348	28 (8.0)	0.96 (0.61,1.49)	0.846
Low RH	208	9 (4.3)	0.54 (0.27,1.08)	0.082
High RH	211	20 (9.5)	1.30 (0.78,2.16)	0.319
Low plus High RH	419	29 (6.9)	0.84 (0.53,1.32)	0.445

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	0.91 (0.58,1.44)	0.698
Low RH	207	0.52 (0.26,1.06)	0.071
High RH	209	1.46 (0.85,2.50)	0.169
Low plus High RH	416	0.87 (0.55,1.40)	0.576

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-55. Analysis of Protein Profile: C4 Complement (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	22 (8.6)	1.03 (0.87,1.22)	0.740
Medium	256	15 (5.9)		
High	255	20 (7.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
762	1.20 (0.96,1.49)	0.097

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.46   Protein Profile: Haptoglobin (Continuous)

A significant overall difference between Ranch Hands and Comparisons was seen in the unadjusted and adjusted Model 1 analyses of haptoglobin in its continuous form (Table 13-56(a,b): difference of means=7.9 mg/dL, p=0.005; difference of adjusted means=6.0 mg/dL, p=0.026). Among all participants, the adjusted mean haptoglobin value was greater for Ranch Hands than for Comparisons (123.3 mg/dL versus 117.3 mg/dL). Stratifying the unadjusted and adjusted analyses by military occupation revealed a significant difference between Ranch Hand and Comparison enlisted groundcrew (Table 13-56(a,b): difference of means=11.2 mg/dL, p=0.010; difference of adjusted means=9.1 mg/dL, p=0.031). Ranch Hand enlisted groundcrew had a greater adjusted mean haptoglobin value than Comparison enlisted groundcrew (132.6 mg/dL versus 123.4 mg/dL).

No significant association with initial dioxin was seen in the unadjusted Model 2 analysis of haptoglobin in its continuous form (Table 13-56(c): p=0.967). The adjusted Model 2 analysis, however, revealed a significant inverse relation between initial dioxin and haptoglobin (Table 13-56(d): Adjusted Slope=-0.227, p=0.043). Ranch Hands in the low, medium, and high dioxin categories had adjusted mean haptoglobin values of 114.7 mg/dL, 120.4 mg/dL, and 107.7 mg/dL, respectively.

The unadjusted Model 3 analysis of haptoglobin revealed three significant contrasts (Table 13-56(e): difference of means=11.4 mg/dL, p=0.013 for Ranch Hands in the low dioxin category versus Comparisons; difference of means=13.8 mg/dL, p=0.003 for Ranch Hands in the high dioxin category versus Comparisons; difference of means=12.6 mg/dL, p<0.001 for Ranch Hands in the low and high dioxin categories combined versus Comparisons). After adjusting for covariates, one contrast remained significant (Table 13-56(f): difference of adjusted means=6.9 mg/dL, p=0.040 for Ranch Hands in the low and high dioxin categories combined versus Comparisons). All remaining unadjusted and adjusted contrasts were nonsignificant (Table 13-56(e,f): p>0.07 for each contrast). Ranch Hands in the low and

high dioxin categories combined had a higher adjusted mean haptoglobin value than Comparisons (124.2 mg/dL versus 117.3 mg/dL, respectively).

No significant associations between 1987 dioxin and haptoglobin in its continuous form were seen in the unadjusted and adjusted Model 4 analyses (Table 13-56(g,h): p>0.07 for each analysis).

Table 13-56. Analysis of Protein Profile: Haptoglobin (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*126.9*	*7.9*	*0.005***
	Comparison	*1,154*	*119.0*		
Officer	Ranch Hand	305	114.5	5.6	0.184
	Comparison	459	108.9		
Enlisted Flyer	Ranch Hand	133	136.1	4.2	0.559
	Comparison	181	132.0		
Enlisted Groundcrew	Ranch Hand	330	135.1	11.2	0.010**
	Comparison	514	123.9		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

**: Statistically significant (p-value≤0.010).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*123.3*	*6.0*	*0.026***
	Comparison	*1,149*	*117.3*		
Officer	Ranch Hand	304	109.8	4.8	0.236
	Comparison	459	105.0		
Enlisted Flyer	Ranch Hand	132	126.5	1.0	0.887
	Comparison	179	125.5		
Enlisted Groundcrew	Ranch Hand	327	132.6	9.1	0.031*
	Comparison	511	123.4		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

*: Statistically significant (0.010<p-value≤0.050).

Table 13-56. Analysis of Protein Profile: Haptoglobin (mg/dL) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	124.6	125.0	0.009	-0.004 (0.099)	0.967
Medium	141	140.6	140.8			
High	140	131.2	130.6			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of haptoglobin versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	114.7	0.129	-0.227 (0.112)	0.043*
Medium	140	120.4			
High	138	107.7			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of haptoglobin versus log_2 (initial dioxin).

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-56. Analysis of Protein Profile: Haptoglobin (mg/dL) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	119.0	119.0		
Background RH	348	120.5	121.3	2.3	0.536
Low RH	208	130.7	130.4	11.4	0.013*
High RH	211	133.6	132.8	13.8	0.003**
Low plus High RH	419	132.1	131.6	12.6	<0.001**

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

*: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	117.3		
Background RH	346	122.1	4.8	0.187
Low RH	207	125.2	7.9	0.073
High RH	209	123.2	5.9	0.186
Low plus High RH	416	124.2	6.9	0.040*

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-56. Analysis of Protein Profile: Haptoglobin (mg/dL) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	118.1	0.004	0.108 (0.061)	0.076
Medium	256	127.2			
High	255	135.4			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of haptoglobin versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	119.6	0.092	-0.065 (0.070)	0.348
Medium	255	123.1			
High	252	122.5			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of haptoglobin versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.47   Protein Profile: Haptoglobin (Discrete)

All unadjusted and adjusted Model 1, 3, and 4 analyses did not show any significant associations between either group or dioxin and haptoglobin in its discrete form (Table 13-57(a,b,e-h): p>0.05 for each analysis).

The unadjusted Model 2 results were nonsignificant (Table 13-57(c): p=0.156). After covariate adjustment, however, a significant inverse relation was revealed between initial dioxin and haptoglobin in its discrete form (Table 13-57(d): Adjusted RR=0.75, p=0.026). The percentages of abnormally high haptoglobin values in the low, medium, and high initial dioxin categories were 13.0, 19.9, and 10.7, respectively.

Table 13-57. Analysis of Protein Profile: Haptoglobin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*107 (13.9)*	*1.23 (0.94,1.62)*	*0.134*
	Comparison	*1,154*	*134 (11.6)*		
Officer	Ranch Hand	305	30 (9.8)	1.17 (0.71,1.94)	0.527
	Comparison	459	39 (8.5)		
Enlisted Flyer	Ranch Hand	133	28 (21.1)	1.66 (0.92,3.01)	0.093
	Comparison	181	25 (13.8)		
Enlisted Groundcrew	Ranch Hand	330	49 (14.8)	1.11 (0.75,1.64)	0.616
	Comparison	514	70 (13.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*1.14 (0.86,1.51)*	*0.370*
Officer	763	1.18 (0.71,1.95)	0.526
Enlisted Flyer	311	1.45 (0.78,2.68)	0.236
Enlisted Groundcrew	838	1.00 (0.66,1.51)	0.998

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	18 (13.0)	0.86 (0.69,1.06)	0.156
Medium	141	28 (19.9)		
High	140	15 (10.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	0.75 (0.58,0.97)	0.026*

[a]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Table 13-57. Analysis of Protein Profile: Haptoglobin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	134 (11.6)		
Background RH	348	45 (12.9)	1.14 (0.79,1.63)	0.492
Low RH	208	34 (16.3)	1.49 (0.99,2.24)	0.058
High RH	211	27 (12.8)	1.11 (0.71,1.73)	0.639
Low plus High RH	419	61 (14.6)	1.28 (0.92,1.78)	0.135

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	1.21 (0.83,1.77)	0.328
Low RH	207	1.35 (0.88,2.07)	0.175
High RH	209	0.87 (0.55,1.39)	0.562
Low plus High RH	416	1.08 (0.77,1.52)	0.652

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	31 (12.1)	0.98 (0.87,1.12)	0.810
Medium	256	37 (14.5)		
High	255	38 (14.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
762	0.89 (0.76,1.03)	0.111

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.48 Protein Profile: Transferrin (Continuous)

The unadjusted and adjusted Model 1 and 2 analyses of transferrin in its continuous form were nonsignificant (Table 13-58(a-d): p>0.24 for each analysis).

The unadjusted Model 3 analysis of transferrin revealed two significant contrasts (Table 13-58(e): difference of means=6.1 mg/dL, p=0.046, for Ranch Hands in the high dioxin category versus Comparisons; difference of means=5.9 mg/dL, p=0.011, for Ranch Hands in the low and high dioxin categories combined versus Comparisons). After adjusting for covariates, a significant difference between Ranch Hands in the low dioxin category and Comparisons was revealed (Table 13-58(f): difference of adjusted means=6.7 mg/dL, p=0.027). The adjusted mean transferrin level for Ranch Hands in the low dioxin category was 254.3 mg/dL versus 247.6 mg/dL for Comparisons. All remaining unadjusted and adjusted Model 3 contrasts were nonsignificant (Table 13-58(e,f): p>0.05 for each contrast).

The unadjusted Model 4 analysis revealed a significant positive association between 1987 dioxin and the continuous form of transferrin (Table 13-58(g): Slope=0.013, p<0.001). The relation was no longer significant, however, after adjusting for covariates (Table 13-58(h): p=0.057).

Table 13-58. Analysis of Protein Profile: Transferrin (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*255.4*	*1.5*	*0.441*
	Comparison	*1,154*	*253.9*		
Officer	Ranch Hand	305	249.7	-1.2	0.684
	Comparison	459	250.9		
Enlisted Flyer	Ranch Hand	133	257.7	3.1	0.510
	Comparison	181	254.7		
Enlisted Groundcrew	Ranch Hand	330	259.8	3.4	0.242
	Comparison	514	256.4		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 13-58. Analysis of Protein Profile: Transferrin (mg/dL) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*763*	*249.1*	*1.3*	*0.469*
	Comparison	*1,149*	*247.8*		
Officer	Ranch Hand	304	244.4	-0.9	0.743
	Comparison	459	245.3		
Enlisted Flyer	Ranch Hand	132	251.9	3.7	0.418
	Comparison	179	248.2		
Enlisted Groundcrew	Ranch Hand	327	251.9	2.6	0.359
	Comparison	511	249.4		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	257.7	257.8	0.002	0.005 (0.006)	0.390
Medium	141	262.7	262.7			
High	140	260.2	260.1			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of transferrin versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	255.8	0.028	-0.002 (0.007)	0.752
Medium	140	257.8			
High	138	251.5			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of transferrin versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 13-58. Analysis of Protein Profile: Transferrin (mg/dL) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,154	253.9	253.9		
Background RH	348	249.7	250.2	-3.7	0.132
Low RH	208	259.9	259.7	5.8	0.058
High RH	211	260.5	260.0	6.1	0.046*
Low plus High RH	419	260.2	259.8	5.9	0.011*

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,149	247.6		
Background RH	346	245.4	-2.2	0.360
Low RH	207	254.3	6.7	0.027*
High RH	209	249.8	2.2	0.471
Low plus High RH	416	252.0	4.4	0.055

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-58. Analysis of Protein Profile: Transferrin (mg/dL) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	248.5	0.019	0.013 (0.004)	<0.001**
Medium	256	256.8			
High	255	261.0			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of transferrin versus log_2 (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	255	250.7	0.043	0.008 (0.004)	0.057
Medium	255	257.7			
High	252	257.2			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of transferrin versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.49   *Protein Profile: Transferrin (Discrete)*

No significant associations between either group or dioxin and transferrin in its discrete form were seen in the unadjusted and adjusted Model 1 and 2 analyses (Table 13-59(a-d): p>0.14 for each analysis).

The unadjusted Model 3 analysis showed a significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 13-59(e): Unadjusted RR=0.48, p=0.017). After adjusting for covariates, two contrasts were significant (Table 13-59(f): Adjusted RR=0.41, p=0.041, for Ranch Hands in the low dioxin category versus Comparisons; Adjusted RR=0.50, p=0.029, for Ranch Hands in the low and high dioxin categories combined versus Comparisons). Comparisons had a higher percentage of abnormally low transferrin values (6.2%) than Ranch Hands in either the low dioxin category (2.9%) or the low and high dioxin categories combined (3.1%). The remaining unadjusted and adjusted Model 3 contrasts were nonsignificant (Table 13-59(e,f): p>0.06 for each contrast).

A significant inverse association was seen between transferrin in its discrete form and 1987 dioxin in the unadjusted Model 4 analysis (Table 13-59(g): Unadjusted RR=0.79, p=0.021). The results were nonsignificant in the adjusted Model 4 analysis (Table 13-59(h): p=0.120).

Table 13-59. Analysis of Protein Profile: Transferrin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*42 (5.5)*	*0.87 (0.59,1.29)*	*0.482*
	Comparison	*1,154*	*72 (6.2)*		
Officer	Ranch Hand	305	21 (6.9)	0.95 (0.54,1.68)	0.872
	Comparison	459	33 (7.2)		
Enlisted Flyer	Ranch Hand	133	6 (4.5)	0.49 (0.19,1.28)	0.145
	Comparison	181	16 (8.8)		
Enlisted Groundcrew	Ranch Hand	330	15 (4.5)	1.02 (0.52,1.98)	0.961
	Comparison	514	23 (4.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,912*	*0.87 (0.59,1.29)*	*0.494*
Officer	763	0.94 (0.53,1.67)	0.841
Enlisted Flyer	311	0.48 (0.18,1.28)	0.141
Enlisted Groundcrew	838	1.07 (0.55,2.09)	0.849

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	5 (3.6)	1.32 (0.90,1.93)	0.169
Medium	141	1 (0.7)		
High	140	7 (5.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.36 (0.86,2.15)	0.187

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with an abnormally low transferrin level.

Table 13-59. Analysis of Protein Profile: Transferrin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	72 (6.2)		
Background RH	348	29 (8.3)	1.37 (0.87,2.15)	0.174
Low RH	208	6 (2.9)	0.45 (0.19,1.04)	0.062
High RH	211	7 (3.3)	0.51 (0.23,1.14)	0.100
Low plus High RH	419	13 (3.1)	0.48 (0.26,0.88)	0.017*

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,149		
Background RH	346	1.30 (0.82,2.07)	0.266
Low RH	207	0.41 (0.18,0.97)	0.041*
High RH	209	0.62 (0.27,1.40)	0.247
Low plus High RH	416	0.50 (0.27,0.93)	0.029*

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-59. Analysis of Protein Profile: Transferrin (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	22 (8.6)	0.79 (0.64,0.97)	0.021*
Medium	256	12 (4.7)		
High	255	8 (3.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
762	0.83 (0.65,1.05)	0.120

[a]Relative risk for a twofold increase in 1987 dioxin.

13.2.2.3.50 Prothrombin Time (Continuous)

In the unadjusted and adjusted Model 1 and 2 analyses of continuous prothrombin time, no significant relations with either group or dioxin were seen (Table 13-60(a-d): p>0.13 for each analysis).

Both the unadjusted and adjusted Model 3 analysis of prothrombin time revealed a significant difference between Ranch Hands in the background dioxin category and Comparisons (Table 13-60(e,f): difference of means=0.08 seconds, p=0.025; difference of adjusted means=0.07 seconds, p=0.042). Ranch Hands in the background dioxin category had a higher adjusted mean prothrombin time than Comparisons (10.79 seconds versus 10.72 seconds, respectively). The remaining unadjusted and adjusted Model 3 contrasts were nonsignificant (Table 13-60(e,f): p≥0.40 for each contrast).

A significant inverse association was seen between 1987 dioxin and prothrombin time in the unadjusted and adjusted Model 4 analyses (Table 13-60(g,h): Slope=-0.002, p=0.044; Adjusted Slope=-0.003, p=0.050). The adjusted mean prothrombin times in the low, medium, and high 1987 dioxin categories were 10.79 seconds, 10.73 seconds, and 10.66 seconds, respectively.

Table 13-60. Analysis of Prothrombin Time (seconds) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*572*	*10.74*	*0.04*	*0.183*
	Comparison	*894*	*10.71*		
Officer	Ranch Hand	224	10.78	0.04	0.338
	Comparison	350	10.74		
Enlisted Flyer	Ranch Hand	91	10.74	0.02	0.758
	Comparison	135	10.72		
Enlisted Groundcrew	Ranch Hand	257	10.71	0.04	0.373
	Comparison	409	10.67		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*569*	*10.76*	*0.04*	*0.131*
	Comparison	*892*	*10.72*		
Officer	Ranch Hand	224	10.77	0.04	0.325
	Comparison	350	10.72		
Enlisted Flyer	Ranch Hand	90	10.75	0.03	0.703
	Comparison	135	10.72		
Enlisted Groundcrew	Ranch Hand	255	10.77	0.05	0.269
	Comparison	407	10.72		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 13-60. Analysis of Prothrombin Time (seconds) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	91	10.78	10.78	0.013	-0.001 (0.002)	0.524
Medium	108	10.67	10.67			
High	103	10.69	10.69			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of prothrombin time versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	91	10.75	0.095	0.001 (0.002)	0.750
Medium	107	10.66			
High	102	10.71			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of prothrombin time versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	894	10.71	10.71		
Background RH	269	10.78	10.79	0.08	0.025*
Low RH	145	10.74	10.73	0.02	0.522
High RH	157	10.68	10.67	-0.04	0.482
Low plus High RH	302	10.71	10.70	-0.01	0.950

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	892	10.72		
Background RH	268	10.79	0.07	0.042*
Low RH	144	10.75	0.03	0.400
High RH	156	10.72	0.00	0.999
Low plus High RH	300	10.73	0.01	0.592

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	193	10.79	0.007	-0.002 (0.001)	0.044*
Medium	187	10.77			
High	191	10.67			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of prothrombin time versus log$_2$ (1987 dioxin).

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

Table 13-60. Analysis of Prothrombin Time (seconds) (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	193	10.79	0.036	-0.003 (0.001)	0.050*
Medium	186	10.73			
High	189	10.66			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of prothrombin time versus log$_2$ (1987 dioxin).

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

13.2.2.3.51 Prothrombin Time (Discrete)

All unadjusted and adjusted Model 1 through 4 analyses of prothrombin time in its discrete form were nonsignificant (Table 13-61(a-h): p>0.13 for each analysis).

Table 13-61. Analysis of Prothrombin Time (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*572*	*5 (0.9)*	*0.98 (0.32,3.00)*	*0.967*
	Comparison	*894*	*8 (0.9)*		
Officer	Ranch Hand	224	2 (0.9)	1.04 (0.17,6.29)	0.964
	Comparison	350	3 (0.9)		
Enlisted Flyer	Ranch Hand	91	2 (2.2)	0.99 (0.16,6.04)	0.990
	Comparison	135	3 (2.2)		
Enlisted Groundcrew	Ranch Hand	257	1 (0.4)	0.79 (0.07,8.81)	0.852
	Comparison	409	2 (0.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,461*	*0.85 (0.26,2.76)*	*0.792*
Officer	574	0.98 (0.16,6.16)	0.982
Enlisted Flyer	225	0.77 (0.12,5.12)	0.786
Enlisted Groundcrew	662	0.80 (0.07,9.25)	0.859

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Table 13-61. Analysis of Prothrombin Time (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	91	3 (3.3)	0.64 (0.27,1.56)	0.275
Medium	108	0 (0.0)		
High	103	1 (1.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
300	0.38 (0.09,1.58)	0.137

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for current alcohol use and current cigarette smoking because of the sparse number of Ranch Hands with an abnormally high prothrombin time.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	894	8 (0.9)		
Background RH	269	1 (0.4)	0.51 (0.06,4.14)	0.529
Low RH	145	3 (2.1)	1.69 (0.41,6.96)	0.465
High RH	157	1 (0.6)	0.55 (0.07,4.50)	0.578
Low plus High RH	302	4 (1.3)	0.94 (0.24,3.78)	0.935

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 13-61. Analysis of Prothrombin Time (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	892		
Background RH	268	0.46 (0.05,3.81)	0.468
Low RH	144	1.47 (0.35,6.15)	0.596
High RH	156	0.59 (0.06,5.60)	0.644
Low plus High RH	300	0.91 (0.21,3.97)	0.903

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	193	1 (0.5)	0.94 (0.54,1.61)	0.814
Medium	187	3 (1.6)		
High	191	1 (0.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
568	0.65 (0.30,1.41)	0.294

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for current alcohol use and current cigarette smoking because of the sparse number of Ranch Hands with an abnormally high prothrombin time.

13.3 DISCUSSION

Digestive symptoms are frequently nonspecific and intermittent; therefore, it is often difficult for physicians to make an accurate diagnosis, particularly with regard to hepatic disease. Liver disorders are commonly asymptomatic; if symptoms are present, they tend to be vague. A physical examination is often misleading or unhelpful. For example, the detection of liver enlargement is often unreliable,

especially in overweight or obese patients. In the case of obstructive airway disease, hyperinflation of the lungs and flattening of the diaphragm may cause the liver's edge to descend abnormally below the right costal margin, resulting in a mistaken diagnosis of hepatomegaly. In addition, detecting the span of the liver using palpation or percussion is often an unreliable index of liver size. If cost is not an issue, the best way to measure liver size is through imaging test screening, such as ultrasound or, preferably, abdominal computed axial tomography (CAT) scan or magnetic resonance imaging (MRI) of the abdomen.

Laboratory testing is the most reliable way to collect data on acute liver disease. The four hepatic enzymes analyzed in the AFHS (AST, ALT, GGT, and LDH) are routinely ordered when evaluating patients who are suspected as having liver disorders. The GGT levels are the most sensitive, although they are typically abnormal in certain circumstances, such as when alcohol is in the patient's system or when the patient is obese. Incidentally, obesity is the single most common cause of abnormal liver tests conducted in the United States (98).

Hepatic enzymes are typically analyzed to detect and follow-up on parenchymal liver diseases, such as alcoholic liver disease, viral hepatitis, and fatty liver due to obesity, diabetes mellitus, or hyperlipidemia. Serum alkaline phosphatase and bilirubin are typically monitored to evaluate cholestatic or obstructive liver diseases, such as those seen in pancreatic cancer, common bile duct stones, or biliary disease in general. Serum alkaline phosphatase levels may be elevated due to other organ dysfunction, primarily attributable to bone-derived alkaline phosphatase. An elevated alkaline phosphatase level is not necessarily indicative of liver disease and may occur in other instances, such as bone growth, Paget's disease (estimated to affect 3% of males over age 40), a neoplasm with metastases to bone, and congestive heart failure.

Similarly, bilirubin measurements can be affected by abnormalities other than intrinsic liver disease. The most common cause of elevated bilirubin is Gilbert's syndrome, which occurs in more than 5 percent of the population and almost 10 percent of males. Gilbert's syndrome causes an elevated indirect bilirubin level, primarily without elevating the direct bilirubin level. The result, then, is an elevated total bilirubin level. In addition, many medications, including over-the-counter drugs, have been implicated in the overproduction of bilirubin that may occur due to hemolysis associated with glucose-six-phosphate dehydrogenase deficiency, a condition that may be present in up to 15 percent of Black males.

Numerous dependent variable-covariate associations that were significant in the AFHS were consistent with associations well recognized in the literature. For instance, older participants in the AFHS had a higher percentage of antibodies for hepatitis A than younger participants. It has been well established that the presence of IgG hepatitis A antibody increases with age in the U.S. population (99). A second important covariate was the increased prevalence of liver disorders, antibodies for hepatitis A, prior hepatitis B infections, and antibodies for hepatitis C in AFHS Black participants compared to non-Black participants. These findings among the U.S. population were reported previously when race was evaluated for liver disease, prevalence of chronic hepatitis C, and prevalence of hepatocellular carcinoma (100, 101). The positive association between race and creatine phosphokinase levels has been well established, with Black participants having higher creatine phosphokinase levels than non-Black participants. This large gap between Black participants and non-Black participants narrows as both cohorts adopt an exercise regimen.

The body mass index covariate revealed a positive association with AST, GGT, C4 complement, haptoglobin, and transferrin. Obese participants showed more occurrences of nonalcohol-related chronic liver disease and cirrhosis, other liver disorders, hepatomegaly, and abnormal α-2-macroglobulin values

than participants who were not obese. The same correlation to obesity has been reported among the general U.S. population (102, 103).

As expected, current alcohol use was associated with elevations of ALT, cholesterol, and other laboratory tests. Heavier drinkers had a greater percentage of abnormally high direct bilirubin values than did lighter drinkers. The GGT level was increased in patients with a lifetime alcohol history; the heaviest lifetime drinkers had the highest percentage of abnormal GGT levels. The frequencies of alcohol-related liver disease and cirrhosis, enlarged liver, prior hepatitis B infection, and antibodies for hepatitis C were all greater among the heaviest lifetime drinkers. All of these findings were reported previously in the general U.S. population (103).

In the 2002 follow-up examination, after adjusting for covariates, there were significant increases for subsets of Ranch Hands relative to Comparisons in the percentage of abnormally high alkaline phosphatase values, elevated triglyceride values, and abnormally high α-1-antitrypsin values. Mean C4 complement levels were significantly lower in Ranch Hands and mean haptoglobin and prothrombin time levels were significantly higher. Ranch Hand groundcrew had a significantly higher percentage of abnormally elevated alkaline phosphatase levels, as well as abnormally high triglyceride levels, relative to Comparisons. These significant results, when examined collectively, do not appear to represent a significant association with liver disease and do not provide evidence for liver disease associated with herbicide exposure or dioxin body burden. One cannot confirm with certainty, however, the cause of these abnormal alkaline phosphatase and triglyceride values. In general, the alkaline phosphatase level is elevated in infiltrative or cholestatic liver disorders, most commonly fatty liver due to diabetes, obesity, or hyperlipidemia and less commonly due to homeostatic drug injury, primary biliary cirrhosis, or bile duct obstruction.

The elevations of two protein variables—α-1-antitrypsin and haptoglobin—yielded statistically significant overall differences, with Ranch Hands adversely affected. In both instances, however, the prevalence of abnormalities was similar in each cohort. There is no known association between liver disease and high α-1-antitrypsin levels or high haptoglobin levels (low α-1-antitrypsin levels, however, are associated with a hereditary form of a liver disorder).

Likewise, a lower mean C4 complement value was seen in Ranch Hand officers and for extrapolated initial dioxin within Ranch Hands. As initial dioxin increased, C4 complement values decreased. The presence of lower mean C4 complement values has no clinically significant meaning. In general, patients with cirrhosis of the liver may have lower complement values, but these are typically seen in association with overall diminishment of protein albumin and prothrombin production. Therefore, if cirrhosis was present, it is unlikely that lower complement values would be seen as an isolated laboratory value abnormality.

The significantly higher mean prothrombin time seen in Ranch Hands in the background dioxin category was not clinically significant and has no known association with significant liver disease in the range of values noted. Prolongation of a prothrombin time typically has clinical significance if there is an increase of at least 2 seconds and preferably 4 seconds in prothrombin time above control.

Although no overall group differences were defined in analyses of both continuous and discrete forms of the data, previous analysis yielded elevations of ALT, AST, and GGT associated with 1987 dioxin levels. The current analysis shows association with serum alkaline phosphatase levels, triglyceride levels, and protein levels, as described above. The alkaline phosphatase, triglycerides, and protein results, while consistent with a dose-response effect, may be explained on the basis of hyperlipidemia and fatty

infiltration of the liver in association with obesity. A causal relation with prior dioxin exposure remains to be established.

In summary, the dependent variable-covariate associations reported have, in general, also been reported in the U.S. population as a whole. These include the association with current and lifetime alcohol consumption, race differences—especially those seen in Black males, the association of liver test abnormalities with body mass index, and the presence of antibodies against hepatitis A associated with age. There was no clear relation between herbicide exposure or dioxin and any of the abnormalities, although based on the analysis of triglycerides, a subtle relation between dioxin and lipid metabolism cannot be excluded.

13.4 SUMMARY

The gastrointestinal assessment was based on data gathered from the participant questionnaire and subsequently verified by a review of medical records, physical examination, and laboratory. Associations with herbicide exposure (i.e., group – Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable in the gastrointestinal assessment. The significant adjusted results are discussed in the sections below.

13.4.1 Model 1: Group Analysis

Among all participants, Ranch Hands had a significantly greater percentage of abnormal triglyceride values and a higher mean haptoglobin level than did Comparisons. The prevalence of prior hepatitis B infection, hepatitis C, and abnormal direct bilirubin values was lower among Ranch Hands than Comparisons.

Positive stool hemoccult results were more prevalent among Ranch Hand officers than Comparison officers. In addition, Ranch Hand officers had a significantly lower mean C4 complement level than did Comparison officers. Ranch Hand officers, however, had a significantly lower mean serum amylase level and significantly fewer abnormal serum amylase values than Comparison officers. Ranch Hand officers also had fewer occurrences of prior hepatitis B infections than did Comparison officers.

Among enlisted groundcrew, Ranch Hands had significantly greater percentages of abnormal alkaline phosphatase and triglyceride values than Comparisons. Ranch Hand enlisted groundcrew had a significantly higher mean haptoglobin level than did Comparison enlisted groundcrew. Fewer occurrences of prior hepatitis B infection were seen among Ranch Hand enlisted groundcrew than among Comparison enlisted groundcrew.

The results of the group analysis are provided in Table 13-62.

Table 13-62. Summary of Group Analysis (Model 1) for Gastrointestinal Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Uncharacterized Hepatitis (D)	NS	ns	NS	NS
Jaundice (unspecified) (D)	ns	ns	NS	ns
Chronic Liver Disease and Cirrhosis (alcohol-related) (D)	NS	NS	NS	ns
Chronic Liver Disease and Cirrhosis (nonalcohol-related) (D)	NS	NS	ns	NS
Liver Abscess and Sequelae of Chronic Liver Disease (D)	NS	NS	--	NS
Enlarged Liver (hepatomegaly) (D)	ns	NS	NS	ns
Other Disorders of the Liver (D)	NS	NS	NS	NS
Physical Examination				
Current Hepatomegaly (D)	NS	NS	ns	NS
Laboratory				
AST (C)	NS	NS	ns	NS
AST (D)	NS	NS	NS	ns
ALT (C)	NS	NS	ns	ns
ALT (D)	ns	NS	ns	ns
GGT (C)	ns	NS	ns	NS
GGT (D)	ns	NS	ns	ns
Alkaline Phosphatase (C)	p=0.048 (2.26)	NS	NS	NS
Alkaline Phosphatase (D)	NS	NS	NS	p=0.031 (1.73)
Total Bilirubin (C)	NS	ns	NS	NS
Total Bilirubin (D)	ns	NS	NS	ns
Direct Bilirubin (D)	ns	ns	--	ns
LDH (C)	NS	p=0.049 (4.1)	NS	NS
LDH (D)	NS	NS	NS	ns
Cholesterol (C)	ns	ns	ns	ns
Cholesterol (D)	ns	ns	NS	ns
HDL Cholesterol (C)[a]	ns	NS	NS	ns
HDL Cholesterol (D)	NS	NS	ns	NS
Cholesterol-HDL Ratio (C)	ns	ns	ns	NS
Cholesterol-HDL Ratio (D)	ns	ns	ns	NS
Triglycerides (C)	NS	NS	ns	NS
Triglycerides (D)	p=0.015 (1.43)	NS	NS	p=0.015 (1.62)
Creatine Phosphokinase (C)	NS	NS	ns	NS
Creatine Phosphokinase (D)	ns	ns	ns	ns
Serum Amylase (C)	ns	ns	ns	NS
Serum Amylase (D)	ns	p=0.042 (0.28)	NS	NS
Antibodies for Hepatitis A (D)	ns	ns	NS	ns
Serological Evidence of Prior Hepatitis B Infection (D)	p<0.001 (0.56)	p=0.039 (0.41)	ns	p=0.017 (0.57)
Antibodies for Hepatitis C (D)	p=0.046 (0.39)	ns	ns	ns
Stool Hemoccult (D)	NS	p=0.041 (9.12)	NS	ns
Protein Profile: Prealbumin (C)[a]	NS	NS	NS	NS

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Protein Profile: Prealbumin (D)	NS	NS	ns	NS
Protein Profile: Albumin (C)[a]	NS	ns	NS	NS
Protein Profile: Albumin (D)	NS	NS	NS	ns
Protein Profile: α-1-Acid Glycoprotein (C)	NS	ns	NS	NS
Protein Profile: α-1-Acid Glycoprotein (D)	NS	ns	NS	NS
Protein Profile: α-1-Antitrypsin (C)	NS	NS	NS	NS
Protein Profile: α-1-Antitrypsin (D)				
Low vs. Normal	ns	ns	ns	ns
High vs. Normal	NS	NS	NS	NS
Protein Profile: α-2-Macroglobulin (C)	ns	NS	ns	ns
Protein Profile: α-2-Macroglobulin (D)	ns	NS	ns	ns
Protein Profile: Apolipoprotein B (C)	ns	ns	ns	ns
Protein Profile: Apolipoprotein B (D)	ns	ns	ns	ns
Protein Profile: C3 Complement (C)[a]	NS	NS	ns	NS
Protein Profile: C3 Complement (D)	ns	NS	ns	ns
Protein Profile: C4 Complement (C)[a]	ns	p=0.044 (-0.83)	NS	ns
Protein Profile: C4 Complement (D)	ns	NS	ns	ns
Protein Profile: Haptoglobin (C)	p=0.005 (7.9)	NS	NS	p=0.010 (11.2)
Protein Profile: Haptoglobin (D)	NS	NS	NS	NS
Protein Profile: Transferrin (C)[a]	NS	ns	NS	NS
Protein Profile: Transferrin (D)	ns	ns	ns	NS
Prothrombin Time (C)	NS	NS	NS	NS
Prothrombin Time (D)	ns	NS	ns	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

Variable	ADJUSTED			
	All	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Medical Records				
Uncharacterized Hepatitis (D)	NS	ns	NS	NS
Jaundice (unspecified) (D)	ns	ns	NS	ns
Chronic Liver Disease and Cirrhosis (alcohol-related) (D)	NS	NS	NS	ns
Chronic Liver Disease and Cirrhosis (nonalcohol-related) (D)	NS	NS	ns	NS
Liver Abscess and Sequelae of Chronic Liver Disease (D)	NS	NS	--	NS
Enlarged Liver (hepatomegaly) (D)	ns	NS	NS	ns
Other Disorders of the Liver (D)	NS	NS	NS	NS
Physical Examination				
Current Hepatomegaly (D)	NS	NS	--	NS
Laboratory				
AST (C)	NS	NS	ns	NS
AST (D)	NS	NS	NS	ns
ALT (C)	NS	NS	ns	ns
ALT (D)	ns	NS	ns	ns
GGT (C)	NS	NS	ns	ns
GGT (D)	ns	NS	ns	ns
Alkaline Phosphatase (C)	NS	NS	NS	NS
Alkaline Phosphatase (D)	NS	NS	NS	p=0.039 (1.70)
Total Bilirubin (C)	NS	ns	NS	NS
Total Bilirubin (D)	NS	NS	NS	ns
Direct Bilirubin (D)	p=0.041 (0.24)	ns	--	--
LDH (C)	NS	NS	NS	NS
LDH (D)	NS	NS	NS	ns
Cholesterol (C)	ns	ns	ns	ns
Cholesterol (D)	ns	ns	ns	ns
HDL Cholesterol (C)[a]	ns	NS	NS	ns
HDL Cholesterol (D)	NS	NS	ns	NS
Cholesterol-HDL Ratio (C)	ns	ns	ns	NS
Cholesterol-HDL Ratio (D)	ns	ns	ns	NS
Triglycerides (C)	NS	NS	ns	NS
Triglycerides (D)	p=0.023 (1.40)	NS	NS	p=0.034 (1.54)
Creatine Phosphokinase (C)	NS	NS	ns	NS
Creatine Phosphokinase (D)	ns	ns	ns	ns
Serum Amylase (C)	ns	p=0.049 (-3.25)	ns	NS
Serum Amylase (D)	ns	p=0.038 (0.27)	NS	NS
Antibodies for Hepatitis A (D)	ns	ns	NS	ns
Serological Evidence of Prior Hepatitis B Infection (D)	p<0.001 (0.53)	p=0.034 (0.40)	ns	p=0.016 (0.56)
Antibodies for Hepatitis C (D)	p=0.037 (0.37)	ns	--	ns
Stool Hemoccult (D)	NS	p=0.043 (8.99)	NS	ns
Protein Profile: Prealbumin (C)[a]	NS	NS	NS	NS
Protein Profile: Prealbumin (D)	NS	NS	ns	NS

	ADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Protein Profile: Albumin (C)[a]	NS	ns	NS	NS
Protein Profile: Albumin (D)	NS	NS	NS	ns
Protein Profile: α-1-Acid Glycoprotein (C)	NS	ns	NS	NS
Protein Profile: α-1-Acid Glycoprotein (D)	NS	ns	NS	NS
Protein Profile: α-1-Antitrypsin (C)	NS	NS	ns	NS
Protein Profile: α-1-Antitrypsin (D)				
Low vs. Normal	ns	ns	--	ns
High vs. Normal	NS	NS	NS	NS
Protein Profile: α-2-Macroglobulin (C)	ns	NS	ns	ns
Protein Profile: α-2-Macroglobulin (D)	ns	NS	ns	ns
Protein Profile: Apolipoprotein B (C)	ns	ns	ns	ns
Protein Profile: Apolipoprotein B (D)	ns	ns	ns	ns
Protein Profile: C3 Complement (C)[a]	NS	NS	ns	NS
Protein Profile: C3 Complement (D)	ns	ns	ns	ns
Protein Profile: C4 Complement (C)[a]	ns	p=0.032 (-0.91)	NS	ns
Protein Profile: C4 Complement (D)	ns	NS	ns	ns
Protein Profile: Haptoglobin (C)	p=0.026 (6.0)	NS	NS	p=0.031 (9.1)
Protein Profile: Haptoglobin (D)	NS	NS	NS	NS
Protein Profile: Transferrin (C)[a]	NS	ns	NS	NS
Protein Profile: Transferrin (D)	ns	ns	ns	NS
Prothrombin Time (C)	NS	NS	NS	NS
Prothrombin Time (D)	ns	ns	ns	ns

[a] A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
     C: Continuous form of dependent variable.
     D: Discrete form of dependent variable.

     The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

     A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

13.4.2 Model 2: Initial Dioxin Analysis

As initial dioxin increased, serum amylase, α-1-acid glycoprotein, C4 complement, and haptoglobin decreased. The percentage of Ranch Hands with abnormally low C4 complement values increased with initial dioxin, but the percentage of Ranch Hands with abnormally high haptoglobin decreased. The results of all unadjusted and adjusted Model 2 analyses are summarized in Table 13-63.

Table 13-63. Summary of Initial Dioxin Analysis (Model 2) for Gastrointestinal Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Uncharacterized Hepatitis (D)	NS	NS
Jaundice (unspecified) (D)	ns	ns
Chronic Liver Disease and Cirrhosis (alcohol-related) (D)	p=0.029 (1.46)	NS
Chronic Liver Disease and Cirrhosis (nonalcohol-related) (D)	NS	NS
Liver Abscess and Sequelae of Chronic Liver Disease (D)	NS	NS
Enlarged Liver (hepatomegaly) (D)	ns	ns
Other Disorders of the Liver (D)	NS	NS
Physical Examination		
Current Hepatomegaly (D)	ns	ns
Laboratory		
AST (C)	ns	NS
AST (D)	NS	NS
ALT (C)	NS	NS
ALT (D)	NS	NS
GGT (C)	ns	ns
GGT (D)	ns	ns
Alkaline Phosphatase (C)	NS	ns
Alkaline Phosphatase (D)	NS	NS
Total Bilirubin (C)	p=0.044 (-0.035)	ns
Total Bilirubin (D)	ns	ns
Direct Bilirubin (D)	--	--
LDH (C)	ns	ns
LDH (D)	p=0.028 (0.76)	ns
Cholesterol (C)	NS	ns
Cholesterol (D)	NS	NS
HDL Cholesterol (C)[a]	p=0.012 (-0.024)	ns
HDL Cholesterol (D)	NS	ns
Cholesterol-HDL Ratio (C)	p=0.009 (0.027)	NS
Cholesterol-HDL Ratio (D)	NS	ns
Triglycerides (C)	NS	NS
Triglycerides (D)	NS	NS
Creatine Phosphokinase (C)	NS	ns
Creatine Phosphokinase (D)	ns	ns
Serum Amylase (C)	ns	p=0.031 (-0.036)
Serum Amylase (D)	ns	ns
Antibodies for Hepatitis A (D)	NS	NS
Serological Evidence of Prior Hepatitis B Infection (D)	NS	NS
Antibodies for Hepatitis C (D)	ns	ns

Variable	Unadjusted	Adjusted
Stool Hemoccult (D)	ns	NS
Protein Profile: Prealbumin (C)[a]	p=0.042 (-0.043)	ns
Protein Profile: Prealbumin (D)	NS	NS
Protein Profile: Albumin (C)[a]	ns	ns
Protein Profile: Albumin (D)	--	--
Protein Profile: α-1-Acid Glycoprotein (C)	ns	p<0.001 (-0.038)
Protein Profile: α-1-Acid Glycoprotein (D)	ns	ns
Protein Profile: α-1-Antitrypsin (C)	NS	ns
Protein Profile: α-1-Antitrypsin (D)		
Low vs. Normal	ns	ns
High vs. Normal	ns	ns
Protein Profile: α-2-Macroglobulin (C)	ns	ns
Protein Profile: α-2-Macroglobulin (D)	ns	NS
Protein Profile: Apolipoprotein B (C)	NS	ns
Protein Profile: Apolipoprotein B (D)	NS	NS
Protein Profile: C3 Complement (C)[a]	NS	ns
Protein Profile: C3 Complement (D)	NS	NS
Protein Profile: C4 Complement (C)[a]	ns	p=0.041 (-0.053)
Protein Profile: C4 Complement (D)	p=0.009 (1.43)	p<0.001 (1.80)
Protein Profile: Haptoglobin (C)	ns	p=0.043 (-0.227)
Protein Profile: Haptoglobin (D)	ns	p=0.026 (0.75)
Protein Profile: Transferrin (C)[a]	NS	ns
Protein Profile: Transferrin (D)	NS	NS
Prothrombin Time (C)	ns	NS
Prothrombin Time (D)	ns	ns

[a]A negative slope was considered adverse for this variable.

Note: NS or ns: Not significant (p>0.05).
     C: Continuous form of dependent variable.
     D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

13.4.3   Model 3: Categorized Dioxin Analysis

Ranch Hands in the background dioxin category had a significantly higher mean prothrombin time than did Comparisons. There were fewer occurrences of prior hepatitis B infection, however, in Ranch Hands than in Comparisons.

Ranch Hands in the low dioxin category had greater percentages of abnormally high triglyceride and α-1-antitrypsin values than did Comparisons. There were significantly fewer occurrences of prior hepatitis B infections and abnormally low transferrin levels, however, among Ranch Hands in the low dioxin category than among Comparisons. In addition, Comparisons had significantly lower mean C3 complement and transferrin levels than did Ranch Hands.

Ranch Hands in the high dioxin category had a greater prevalence of abnormally high triglyceride levels than Comparisons.

Ranch Hands in the low and high dioxin categories combined had a higher mean haptoglobin level than Comparisons and a greater percentage of abnormally high triglyceride and α-1-antitrypsin values than Comparisons. Ranch Hands in the low and high dioxin categories combined, however, had fewer occurrences of jaundice and prior hepatitis B infections, as well as fewer abnormally high cholesterol and abnormally low transferrin values than Comparisons.

The results of all unadjusted and adjusted Model 3 analyses are summarized in Table 13-64.

Table 13-64. Summary of Categorized Dioxin Analysis (Model 3) for Gastrointestinal Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Uncharacterized Hepatitis (D)	NS	NS	p=0.045 (2.54)	NS
Jaundice (unspecified) (D)	NS	ns	ns	p=0.024 (0.24)
Chronic Liver Disease and Cirrhosis (alcohol-related) (D)	NS	ns	NS	ns
Chronic Liver Disease and Cirrhosis (nonalcohol-related) (D)	NS	NS	NS	NS
Liver Abscess and Sequelae of Chronic Liver Disease (D)	NS	NS	NS	NS
Enlarged Liver (Hepatomegaly) (D)	ns	ns	ns	ns
Other Disorders of the Liver (D)	NS	NS	NS	NS
Physical Examination				
Current Hepatomegaly (D)	NS	NS	ns	NS
Laboratory				
AST (C)	NS	NS	NS	NS
AST (D)	NS	NS	NS	NS
ALT (C)	ns	NS	NS	NS
ALT (D)	ns	NS	NS	NS
GGT (C)	ns	NS	NS	NS
GGT (D)	ns	NS	ns	NS
Alkaline Phosphatase (C)	NS	NS	p=0.048 (3.69)	p=0.018 (3.34)

	UNADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Alkaline Phosphatase (D)	NS	NS	NS	NS
Total Bilirubin (C)	NS	NS	ns	ns
Total Bilirubin (D)	NS	NS	ns	ns
Direct Bilirubin (D)	ns	ns	ns	ns
LDH (C)	NS	NS	NS	NS
LDH (D)	NS	NS	ns	NS
Cholesterol (C)	p=0.035 (-4.7)	ns	ns	ns
Cholesterol (D)	ns	ns	ns	ns
HDL Cholesterol (C)[a]	NS	ns	p=0.002 (-2.55)	p=0.035 (-1.34)
HDL Cholesterol (D)	NS	NS	NS	NS
Cholesterol-HDL Ratio (C)	p=0.020 (-0.17)	ns	p=0.010 (0.24)	NS
Cholesterol-HDL Ratio (D)	p=0.045 (0.76)	ns	NS	NS
Triglycerides (C)	p=0.045 (-8.2)	NS	p=0.002 (16.6)	p=0.009 (10.6)
Triglycerides (D)	ns	p=0.021 (1.65)	p<0.001 (2.26)	p<0.001 (1.93)
Creatine Phosphokinase (C)	ns	NS	NS	NS
Creatine Phosphokinase (D)	ns	ns	ns	ns
Serum Amylase (C)	ns	NS	ns	ns
Serum Amylase (D)	ns	NS	ns	NS
Antibodies for Hepatitis A (D)	ns	ns	ns	ns
Serological Evidence of Prior Hepatitis B Infection (D)	p<0.001 (0.38)	ns	ns	ns
Antibodies for Hepatitis C (D)	ns	ns	ns	ns
Stool Hemoccult (D)	NS	NS	NS	NS
Protein Profile: Prealbumin (C)[a]	NS	NS	NS	NS
Protein Profile: Prealbumin (D)	NS	NS	NS	NS
Protein Profile: Albumin (C)[a]	ns	NS	NS	NS
Protein Profile: Albumin (D)	NS	ns	ns	ns
Protein Profile: α-1-Acid Glycoprotein (C)	ns	NS	NS	NS
Protein Profile: α-1-Acid Glycoprotein (D)	ns	p=0.044 (1.79)	NS	NS
Protein Profile: α-1-Antitrypsin (C)	ns	p=0.037 (4.1)	NS	p=0.015 (3.6)
Protein Profile: α-1-Antitrypsin (D)				
Low vs. Normal	ns	ns	ns	ns
High vs. Normal	ns	p=0.047 (1.56)	p=0.047 (1.56)	p=0.010 (1.56)
Protein Profile: α-2-Macroglobulin (C)	NS	NS	ns	ns
Protein Profile: α-2-Macroglobulin (D)	ns	NS	ns	ns
Protein Profile: Apolipoprotein B (C)	ns	ns	NS	NS
Protein Profile: Apolipoprotein B (D)	ns	ns	ns	ns
Protein Profile: C3 Complement (C)[a]	ns	p=0.003 (4.7)	p=0.038 (3.2)	p<0.001 (3.9)
Protein Profile: C3 Complement (D)	NS	ns	ns	p=0.034 (*)
Protein Profile: C4 Complement (C)[a]	ns	NS	ns	ns
Protein Profile: C4 Complement (D)	ns	ns	NS	ns
Protein Profile: Haptoglobin (C)	NS	p=0.013 (11.4)	p=0.003 (13.8)	p<0.001 (12.6)

	UNADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Protein Profile: Haptoglobin (D)	NS	NS	NS	NS
Protein Profile: Transferrin (C)[a]	ns	NS	p=0.046 (6.1)	p=0.011 (5.9)
Protein Profile: Transferrin (D)	NS	ns	ns	p=0.017 (0.48)
Prothrombin Time (C)	p=0.025 (0.08)	NS	ns	ns
Prothrombin Time (D)	ns	NS	ns	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

--: The analysis was not performed because of the sparse number of participants with an abnormality.

*: Relative risk could not be calculated. One Ranch Hand in the high dioxin category and 21 Comparisons had an abnormally low C3 complement level.

Note: NS or ns: Not significant (p>0.05).
　　　　C: Continuous form of dependent variable.
　　　　D: Discrete form of dependent variable.

　　　　The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

　　　　A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

	ADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Medical Records				
Uncharacterized Hepatitis (D)	NS	NS	NS	NS
Jaundice (unspecified) (D)	NS	ns	ns	p=0.027 (0.24)
Chronic Liver Disease and Cirrhosis (alcohol-related) (D)	NS	ns	NS	ns
Chronic Liver Disease and Cirrhosis (nonalcohol-related) (D)	NS	NS	NS	NS
Liver Abscess and Sequelae of Chronic Liver Disease (D)	NS	NS	NS	NS
Enlarged Liver (Hepatomegaly) (D)	NS	ns	ns	ns
Other Disorders of the Liver (D)	NS	NS	NS	NS
Physical Examination				
Current Hepatomegaly (D)	NS	NS	ns	NS
Laboratory				
AST (C)	NS	NS	NS	NS

Table 13-64. Summary of Categorized Dioxin Analysis (Model 3) for Gastrointestinal Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
AST (D)	NS	NS	NS	NS
ALT (C)	ns	NS	NS	NS
ALT (D)	ns	NS	ns	ns
GGT (C)	ns	NS	NS	NS
GGT (D)	ns	NS	ns	NS
Alkaline Phosphatase (C)	NS	NS	NS	NS
Alkaline Phosphatase (D)	NS	NS	NS	NS
Total Bilirubin (C)	NS	NS	ns	NS
Total Bilirubin (D)	NS	NS	ns	ns
Direct Bilirubin (D)	ns	--	--	--
LDH (C)	NS	NS	NS	NS
LDH (D)	NS	NS	ns	NS
Cholesterol (C)	ns	ns	ns	ns
Cholesterol (D)	ns	ns	ns	p=0.039 (0.68)
HDL Cholesterol (C)[a]	NS	NS	ns	ns
HDL Cholesterol (D)	NS	NS	NS	NS
Cholesterol-HDL Ratio (C)	ns	ns	NS	ns
Cholesterol-HDL Ratio (D)	ns	ns	NS	ns
Triglycerides (C)	ns	NS	NS	NS
Triglycerides (D)	ns	p=0.015 (1.72)	p=0.012 (1.70)	p=0.001 (1.71)
Creatine Phosphokinase (C)	NS	NS	NS	NS
Creatine Phosphokinase (D)	NS	ns	ns	ns
Serum Amylase (C)	ns	ns	ns	ns
Serum Amylase (D)	ns	ns	ns	ns
Antibodies for Hepatitis A (D)	ns	ns	ns	ns
Serological Evidence of Prior Hepatitis B Infection (D)	p=0.004 (0.44)	p=0.045 (0.56)	ns	p=0.012 (0.59)
Antibodies for Hepatitis C (D)	ns	ns	ns	ns
Stool Hemoccult (D)	NS	NS	ns	ns
Protein Profile: Prealbumin (C)[a]	NS	NS	NS	NS
Protein Profile: Prealbumin (D)	NS	NS	NS	NS
Protein Profile: Albumin (C)[a]	ns	NS	ns	NS
Protein Profile: Albumin (D)	NS	--	--	--
Protein Profile: α-1-Acid Glycoprotein (C)	ns	NS	ns	NS
Protein Profile: α-1-Acid Glycoprotein (D)	ns	NS	NS	NS
Protein Profile: α-1-Antitrypsin (C)	NS	NS	NS	NS
Protein Profile: α-1-Antitrypsin (D)				
Low vs. Normal	ns	ns	ns	ns
High vs. Normal	ns	p=0.042 (1.59)	NS	p=0.030 (1.48)
Protein Profile: α-2-Macroglobulin (C)	NS	NS	ns	ns
Protein Profile: α-2-Macroglobulin (D)	ns	ns	ns	ns
Protein Profile: Apolipoprotein B (C)	ns	ns	ns	ns

| | ADJUSTED | | | |
| | Background Ranch Hands vs. Comparisons | Low Ranch Hands vs. Comparisons | High Ranch Hands vs. Comparisons | Low plus High Ranch Hands vs. Comparisons |
Variable				
Protein Profile: Apolipoprotein B (D)	ns	ns	ns	ns
Protein Profile: C3 Complement (C)[a]	ns	p=0.011 (3.8)	ns	NS
Protein Profile: C3 Complement (D)	ns	--	ns	--
Protein Profile: C4 Complement (C)[a]	ns	NS	ns	ns
Protein Profile: C4 Complement (D)	ns	ns	NS	ns
Protein Profile: Haptoglobin (C)	NS	NS	NS	p=0.040 (6.9)
Protein Profile: Haptoglobin (D)	NS	NS	ns	NS
Protein Profile: Transferrin (C)[a]	ns	p=0.027 (6.7)	NS	NS
Protein Profile: Transferrin (D)	NS	p=0.041 (0.41)	ns	p=0.029 (0.50)
Prothrombin Time (C)	p=0.042 (0.07)	NS	NS	NS
Prothrombin Time (D)	ns	NS	ns	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

13.4.4 Model 4: 1987 Dioxin Level Analysis

The Model 4 analysis showed that the percentage of Ranch Hands with abnormal triglyceride values significantly increased as 1987 dioxin increased. The prevalence of jaundice and abnormally low albumin values decreased with increasing 1987 dioxin. In addition, mean serum amylase and prothrombin time values significantly decreased with increasing 1987 dioxin. All results for Model 4 unadjusted and adjusted analyses are summarized in Table 13-65.

Table 13-65. Summary of 1987 Dioxin Analysis (Model 4) for Gastrointestinal Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Uncharacterized Hepatitis (D)	NS	NS
Jaundice (unspecified) (D)	p=0.004 (0.60)	p=0.014 (0.59)
Chronic Liver Disease and Cirrhosis (alcohol-related) (D)	NS	NS
Chronic Liver Disease and Cirrhosis (nonalcohol-related) (D)	NS	NS
Liver Abscess and Sequelae of Chronic Liver Disease (D)	NS	NS
Enlarged Liver (hepatomegaly) (D)	ns	ns
Other Disorders of the Liver (D)	NS	NS
Physical Examination		
Current Hepatomegaly (D)	ns	ns
Laboratory		
AST (C)	ns	NS
AST (D)	NS	NS
ALT (C)	NS	NS
ALT (D)	NS	NS
GGT (C)	NS	NS
GGT (D)	NS	NS
Alkaline Phosphatase (C)	NS	ns
Alkaline Phosphatase (D)	NS	ns
Total Bilirubin (C)	p=0.040 (-0.022)	ns
Total Bilirubin (D)	ns	ns
Direct Bilirubin (D)	ns	ns
LDH (C)	ns	ns
LDH (D)	ns	ns
Cholesterol (C)	ns	ns
Cholesterol (D)	ns	ns
HDL Cholesterol (C)[a]	p<0.001 (-0.031)	ns
HDL Cholesterol (D)	NS	ns
Cholesterol-HDL Ratio (C)	p<0.001 (0.030)	NS
Cholesterol-HDL Ratio (D)	p<0.001 (1.17)	ns
Triglycerides (C)	p<0.001 (0.060)	NS
Triglycerides (D)	p<0.001 (1.35)	p=0.020 (1.20)
Creatine Phosphokinase (C)	p=0.032 (0.028)	NS
Creatine Phosphokinase (D)	ns	ns
Serum Amylase (C)	p=0.029 (-0.019)	p=0.048 (-0.020)
Serum Amylase (D)	ns	ns
Antibodies for Hepatitis A (D)	NS	NS
Serological Evidence of Prior Hepatitis B Infection (D)	p=0.008 (1.26)	NS
Antibodies for Hepatitis C (D)	ns	ns
Stool Hemoccult (D)	NS	NS
Protein Profile: Prealbumin (C)[a]	ns	ns
Protein Profile: Prealbumin (D)	ns	ns
Protein Profile: Albumin (C)[a]	NS	ns
Protein Profile: Albumin (D)	p=0.015 (0.50)	p=0.030 (0.37)
Protein Profile: α-1-Acid Glycoprotein (C)	NS	ns
Protein Profile: α-1-Acid Glycoprotein (D)	NS	ns

Variable	Unadjusted	Adjusted
Protein Profile: α-1-Antitrypsin (C)	NS	ns
Protein Profile: α-1-Antitrypsin (D)		
Low vs. Normal	ns	ns
High vs. Normal	NS	NS
Protein Profile: α-2-Macroglobulin (C)	ns	ns
Protein Profile: α-2-Macroglobulin (D)	NS	NS
Protein Profile: Apolipoprotein B (C)	NS	ns
Protein Profile: Apolipoprotein B (D)	NS	NS
Protein Profile: C3 Complement (C)[a]	p<0.001 (0.126)	NS
Protein Profile: C3 Complement (D)	p=0.038 (0.64)	ns
Protein Profile: C4 Complement (C)[a]	NS	ns
Protein Profile: C4 Complement (D)	NS	NS
Protein Profile: Haptoglobin (C)	NS	ns
Protein Profile: Haptoglobin (D)	ns	ns
Protein Profile: Transferrin (C)[a]	p<0.001 (0.013)	NS
Protein Profile: Transferrin (D)	p=0.021 (0.79)	ns
Prothrombin Time (C)	p=0.044 (-0.002)	p=0.050 (-0.003)
Prothrombin Time (D)	ns	ns

[a]A negative slope was considered adverse for this variable.

Note: NS or ns: Not significant (p>0.05).
       C: Continuous form of dependent variable.
       D: Discrete form of dependent variable.

       The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

       A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

13.4.5 Summary of Significant Results

Table 13-66 summarizes the significant results (p≤0.05) for the adjusted analyses that were performed for the gastrointestinal assessment. The dependent variable and its table reference are listed, along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and is explained in footnotes.

Table 13-66. Summary of Results from Significant Adjusted Analyses in the Gastrointestinal Assessment

Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Unspecified Jaundice (13-4)	3	Low plus High RH vs. C	0.027	0.24 (0.07,0.85)	RH: 0.7% C: 2.9%	(a)
	4	All RH: 1987 Dioxin	0.014	0.59 (0.39,0.90)	Low: 3.2% Medium: 2.0% High: 0.4%	(b)
Alkaline Phosphatase (13-18)	1	RH vs. C, Enlisted Groundcrew	0.039	1.70 (1.03,2.80)	RH: 10.6% C: 6.4%	(c)
Direct Bilirubin (13-21)	1	RH vs. C, All	0.041	0.24 (0.05,1.14)	RH: 0.3% C: 1.0%	(c)
Cholesterol (13-25)	3	Low plus High RH vs. C	0.039	0.68 (0.47,0.98)	RH: 10.3% C: 13.3%	(a)
Triglycerides (13-31)	1	RH vs. C, All	0.023	1.40 (1.05,1.88)	RH: 13.4% C: 9.8%	(c)
	1	RH vs. C, Enlisted Groundcrew	0.034	1.54 (1.03,2.29)	RH: 17.9% C: 11.9%	(c)
	3	Low RH vs. C	0.015	1.72 (1.11,2.66)	RH: 15.4% C: 9.8%	(a)
	3	High RH vs. C	0.012	1.70 (1.12,2.57)	RH: 20.4% C: 9.8%	(a)
	3	Low plus High RH vs. C	0.001	1.71 (1.23,2.38)	RH: 17.9% C: 9.8%	(a)
	4	All RH: 1987 Dioxin	0.020	1.20 (1.03,1.40)	Low: 6.3% Medium: 12.9% High: 21.2%	(b)
Serum Amylase (13-34)	1	RH vs. C, Officer	0.049	-3.25	RH: 57.85 U/L C: 61.10 U/L	(d)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.031	-0.036 (0.017)	Low: 63.07 U/L Medium: 57.35 U/L High: 57.06 U/L	(e)
	4	All RH: 1987 Dioxin	0.048	-0.020 (0.010)	Low: 63.87 U/L Medium: 62.03 U/L High: 58.26 U/L	(f)
Serum Amylase (13-35)	1	RH vs. C, Officer	0.038	0.27 (0.08,0.93)	RH: 1.0% C: 3.5%	(c)
Prior Hepatitis B Infection (13-37)	1	RH vs. C, All	<0.001	0.53 (0.38,0.76)	RH: 6.4% C: 11.0%	(c)
	1	RH vs. C, Officer	0.034	0.40 (0.17,0.93)	RH: 2.3% C: 5.4%	(c)
	1	RH vs. C, Enlisted Groundcrew	0.016	0.56 (0.35,0.90)	RH: 8.3% C: 13.7%	(c)
	3	Background RH vs. C	0.004	0.44 (0.25,0.77)	RH: 4.3% C: 11.0%	(a)
	3	Low RH vs. C	0.045	0.56 (0.31,0.99)	RH: 7.1% C: 11.0%	(a)
	3	Low plus High RH vs. C	0.012	0.59 (0.40,0.89)	RH: 8.3% C: 11.0%	(a)

Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Antibodies for Hepatitis C (13-38)	1	RH vs. C, All	0.037	0.37 (0.13,1.02)	RH: 0.6% C: 1.6%	(c)
Stool Hemoccult (13-39)	1	RH vs. C, Officer	0.043	8.99 (1.07,75.33)	RH: 2.1% C: 0.2%	(c)
Albumin (13-43)	4	All RH: 1987 Dioxin	0.030	0.37 (0.15,0.94)	Low: 1.6% Medium: 0.4% High: 0.0%	(b)
α-1-Acid Glycoprotein (13-44)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	<0.001	-0.038 (0.010)	Low: 76.97 mg/dL Medium: 76.46 mg/dL High: 71.12 mg/dL	(e)
α-1-Antitrypsin (13-47)	3	Low RH vs. C – Abnormal High vs. Normal	0.042	1.59 (1.02,2.49)	RH: 14.4% C: 9.9%	(a)
	3	Low plus High RH vs. C – Abnormal High vs. Normal	0.030	1.48 (1.04,2.10)	RH: 14.1% C: 9.9%	(a)
C3 Complement[a] (13-52)	3	Low RH vs. C	0.011	3.8	RH: 124.2 mg/dL C: 120.4 mg/dL	(g)
C4 Complement[a] (13-54)	1	RH vs. C, Officer	0.032	-0.91	RH: 23.56 mg/dL C: 24.46 mg/dL	(d)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.041	-0.053 (0.026)	Low: 23.52 mg/dL Medium: 24.47 mg/dL High: 22.90 mg/dL	(h)
C4 Complement (13-55)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	<0.001	1.80 (1.26,2.57)	Low: 5.8% Medium: 3.5% High: 11.4%	(i)
Haptoglobin (13-56)	1	RH vs. C, All	0.026	6.0	RH: 123.3 mg/dL C: 117.3 mg/dL	(d)
	1	RH vs. C, Enlisted Groundcrew	0.031	9.1	RH: 132.6 mg/dL C: 123.4 mg/dL	(d)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.043	-0.227 (0.112)	Low: 114.7 mg/dL Medium: 120.4 mg/dL High: 107.7 mg/dL	(h)
	3	Low plus High RH vs. C	0.040	6.9	RH: 124.2 mg/dL C: 117.3 mg/dL	(g)
Haptoglobin (13-57)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.026	0.75 (0.58,0.97)	Low: 13.0% Medium: 19.9% High: 10.7%	(i)
Transferrin[a] (13-58)	3	Low RH vs. C	0.027	6.7	RH: 254.3 mg/dL C: 247.6 mg/dL	(g)
Transferrin (13-59)	3	Low RH vs. C	0.041	0.41 (0.18,0.97)	RH: 2.9% C: 6.2%	(a)
	3	Low plus High RH vs. C	0.029	0.50 (0.27,0.93)	RH: 3.1% C: 6.2%	(a)
Prothrombin Time (13-60)	3	Background RH vs. C	0.042	0.07	RH: 10.79 seconds C: 10.72 seconds	(g)
	4	All RH: 1987 Dioxin	0.050	-0.003 (0.001)	Low: 10.79 seconds Medium: 10.73 seconds High: 10.66 seconds	(f)

Table 13-66. Summary of Results from Significant Adjusted Analyses in the Gastrointestinal Assessment (Continued)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(d): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each exposure group in contrast.

(e): Continuous variable: slope and standard error were presented and were based on the natural logarithm of the dependent variable versus $\log_2$ (initial dioxin); adjusted means were presented for each of three initial dioxin categories.

(f): Continuous variable: slope and standard error were presented and were based on the natural logarithm of the dependent variable versus $\log_2$ (1987 dioxin); adjusted means were presented for each of three 1987 dioxin categories.

(g): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each dioxin category in contrast.

(h): Continuous variable: slope and standard error were presented and were based on the square root of the dependent variable versus $\log_2$ (initial dioxin); adjusted means were presented for each of three initial dioxin categories.

(i): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal was presented for each of three initial dioxin categories.

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: RH = Ranch Hand.
C = Comparison.

Model 2:   Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt).

Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Model 4:   Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

13.5 CONCLUSION

The gastrointestinal assessment of the AFHS 2002 follow-up examination data consisted of the analysis of (1) 7 categories of liver disorders, which were based on self-reporting by participants and verified by a medical records review, (2) hepatomegaly (enlarged liver), as determined at the 2002 physical examination, and (3) 28 laboratory measurements. Laboratory tests are generally considered the most reliable method for identifying acute liver disease, because digestive symptoms are frequently nonspecific and intermittent and liver disorders are commonly asymptomatic. Furthermore, the detection of liver

enlargement on the sole basis of a physical examination may be confounded by factors such as obesity or obstructive airway disease.

Positive stool hemoccult results were increased and mean C4 complement was decreased among Ranch Hand officers. Among enlisted groundcrew, Ranch Hands had greater percentages of abnormal alkaline phosphatase and triglyceride values than Comparisons. Ranch Hand enlisted groundcrew had a higher mean haptoglobin level.

As initial dioxin increased, C4 complement levels decreased and the percentage of Ranch Hands with abnormally low C4 complement values increased.

Ranch Hands in the low dioxin category, high dioxin category, and low and high dioxin categories combined had increased percentages of abnormally high triglyceride values. Ranch Hands in the low dioxin category and low and high dioxin categories combined had an increased prevalence of abnormally high α-1-antitrypsin values than did Comparisons. In the background dioxin category, Ranch Hands had a higher mean prothrombin time than Comparisons. In the low and high dioxin categories combined, Ranch Hands had a higher mean haptoglobin than Comparisons.

The percentage of Ranch Hands with abnormal triglyceride values significantly increased as 1987 dioxin increased.

There was no clear relation between herbicide exposure or dioxin levels and any of the abnormalities, although based on the analysis of triglycerides, a subtle relation between dioxin and lipid metabolism cannot be excluded.

REFERENCES

1. Institute of Medicine. 2003. Veterans and Agent Orange: Update 2002. National Academy Press: Washington, DC.

2. McNulty, W.P. 1977. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-diozin for rhesus monkeys: Brief report. *Bulletin of Environmental Contamination and Toxicology* 18:108-9.

3. Olson, J.R., M.A. Holscher, and R.A. Neal. 1980. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the golden Syrian hamster. *Toxicology and Applied Pharmacology* 55:67-78.

4. Palmer, J.S., and R.D. Radeleff. 1964. The toxicologic effects of certain fungicides and herbicides on sheep and cattle. *Annals of the New York Academy of Sciences* 11:729-36.

5. Goldstein, J.A., P. Hickman, H. Bergman, and J.G. Vos. 1973. Hepatic porphyria induced by 2,3,7,8-tetrachlorodibenzo-p-dioxin in the mouse. *Research Communications in Chemical Pathology and Pharmacology* 6:919-28.

6. Madhukar, B.V., and F. Matsumura. 1981. Difference in the nature of induction of mixed-function oxidase systems of the rat liver among phenobarbital, DDT, 3-methylcholanthrene, and TCDD. *Toxicology and Applied Pharmacology* 61:109-18.

7. Brooks, A.L., S.W. Jordan, K.K. Bose, J. Smith, and D.C. Allison. 1988. The cytogenetic and hepatotoxic effects of dioxin on mouse liver cells. *Cell Biology and Toxicology* 4:31-40.

8. van Birgelen, A.P., and M. van den Berg. 2000. Toxicokinetics. *Food Additives and Contaminants* 17:267-73.

9. Potter, C.L., I.G. Sipes, and D.H. Russell. 1983. Hypothyroxinemia and hypothermia in rats in response to 2,3,7,8-tetrachlorodibenzo-p-dioxin administration. *Toxicology and Applied Pharmacology* 69:89-95.

10. Theobald, H.M., G.B. Ingall, T.A. Mably, and R.E. Peterson. 1991. Response of the antral mucosa of the rat stomach to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacology* 108:167-79.

11. Norback, D.H., and J.R. Allen. 1973. Biological responses of the nonhuman primate, chicken, and rat to chlorinated dibenzo-p-dioxin ingestion. *Environmental Health Perspectives* 5:233-40.

12. Becker, G.M., and W.P. McNulty. 1984. Gastric epithelial cell proliferation in monkeys fed 3,4,3',4'-tetrachlorobiphenyl. *The Journal of Pathology* 143:267-74.

13. Richter, E., G. Hunder, and W. Forth. 1992. Inhibition of intestinal glucose absorption in rats treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Veterinary and Human Toxicology* 34:123-6.

14. Shen, E.S., S.I. Gutman, and J.R. Olson. 1991. Comparison of 2,3,7,8-tetrachlorodibenzo-p-dioxin-mediated hepatotoxicity in C57BL/6J and DBA/2J mice. *Journal of Toxicology and Environmental Health* 32:367-81.

15. Piper, W.N., J.Q. Rose, and P.J. Gehring. 1973. Excretion and tissue distribution of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the rat. *Environmental Health Perspectives* 5:241-4.

16. Allen, J.R., J.P. Van Miller, and D.H. Norback. 1977. Tissue distribution, excretion, and biological effects of (14C) tetrachlorodibenzo-p-dioxin in rats. *Food and Cosmetic Toxicology* 15:401-10.

17. Tsuda, S., A. Rosenberg, and T. Nakatsugawa. 1988. Translobular uptake patterns of environmental toxicants in the rat liver. *Bulletin of Environmental Contamination and Toxicology* 40:410-7.

18. Lakshman, M.R., B.S. Campbell, S.J. Chirtel, N. Ekarohita, and M. Ezekiel. 1986. Studies on the mechanism of absorption and distribution of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the rat. *Journal of Pharmacology and Experimental Therapeutics* 239:673-7.

19. Pohjanvirta, R., T. Vartiainen, A. Uusi-Rauva, J. Monkkonen, and J. Tuomisto. 1990. Tissue distribution, metabolism, and excretion of 14C-TCDD in a TCDD-susceptible and a TCDD-resistant rat strain. *Pharmacology and Toxicology* 66:93-100.

20. Hagenmaier, H., T. Wiesmuller, G. Golor, R. Krowke, H. Helge, and D. Neubert. 1990. Transfer of various polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDDs and PCDFs) via placenta and through milk in a marmoset monkey. *Archives of Toxicology* 64:601-15.

21. Gehring, P.J., and J.E. Betso. 1978. Phenoxy acids: Effects and fate in mammals. *Ecology Bulletin* 27:122-33.

22. U.S. Environmental Protection Agency. 1984. Health assessment document for polychlorinated dibenzo-p-dioxins. Cincinnati, OH.

23. Dragan, Y.P., X.H. Xu, T.L. Goldsworthy, H.A. Campbell, R.R. Maronpot, and H.C. Pitot. 1992. Characterization of the promotion of altered hepatic foci by 2,3,7,8-tetrachlorodibenzo-p-dioxin in the female rat. *Carcinogenesis* 13:1389-95.

24. Hochstein, M.S., Jr., J.A. Render, S.J. Bursian, and R.J. Aulerich. 2001. Chronic toxicity of dietary 2,3,7,8-tetrachlorodibenzo-p-dioxin to mink. *Veterinary and Human Toxicology* 43:134-9.

25. Mably, T.A., H.M. Theobald, G.B. Ingall, and R.E. Peterson. 1990. Hypergastrinemia is associated with decreased gastric acid secretion in 2,3,7,8-tetrachlorodibenzo-p-dioxin-treated rats. *Toxicology and Applied Pharmacology* 106:518-28.

26. al-Turk, W.A., M.A. Shara, H. Mohammadpour, and S.J. Stohs. 1988. Dietary iron and 2,3,7,8-tetrachlorodibenzo-p-dioxin induced alterations in hepatic lipid peroxidation, glutathione content and body weight. *Drug and Chemical Toxicology* 11:55-70.

27. Shara, M.A., and S.J. Stohs. 1987. Biochemical and toxicological effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) congeners in female rats. *Archives of Environmental Contamination and Toxicology* 16:599-605.

28. Al-Bayati, Z.A., and S.J. Stohs. 1987. The role of iron in 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced lipid peroxidation by rat liver microsomes. *Toxicology Letters* 38:115-21.

29. al-Bayati, Z.A., and S.J. Stohs. 1991. The possible role of phospholipase A2 in hepatic microsomal lipid peroxidation induced by 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Archives of Environmental Contamination and Toxicology* 20:361-5.

30. Lakshman, M.R., P. Ghosh, and S.J. Chirtel. 1991. Mechanism of action of 2,3,7,8-tetrachlorodibenzo-p-dioxin on intermediary metabolism in the rat. *The Journal of Pharmacology and Experimental Therapeutics* 258:317-9.

31. Slezak, B.P., J.T. Hamm, J. Reyna, C.H. Hurst, and L.S. Birnbaum. 2002. TCDD-mediated oxidative stress in male rat pups following perinatal exposure. *Journal of Biochemical and Molecular Toxicology* 16:49-52.

32. Hassoun, E.A., F. Li, A. Abushaban, and S.J. Stohs. 2000. The relative abilities of TCDD and its congeners to induce oxidative stress in the hepatic and brain tissues of rats after subchronic exposure. *Toxicology* 145:103-13.

33. Hassoun, E.A., H. Wang, A. Abushaban, and S.J. Stohs. 2002. Induction of oxidative stress in the tissues of rats after chronic exposure to TCDD, 2,3,4,7,8-pentachlorodibenzofuran, and 3,3',4,4',5-pentachlorobiphenyl. *Journal of Toxicology and Environmental Health Part A* 65:825-42.

34. Hassoun, E.A., F. Li, A. Abushaban, and S.J. Stohs. 2001. Production of superoxide anion, lipid peroxidation and DNA damage in the hepatic and brain tissues of rats after subchronic exposure to mixtures of TCDD and its congeners. *Journal of Applied Toxicology* 21:211-9.

35. Kohli, K.K., and J.A. Goldstein. 1981. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on hepatic and renal prostaglandin synthetase. *Life Sciences* 29:299-305.

36. Vogel, C., A.M. Boerboom, C. Baechle, C. El-Bahay, R. Kahl, G.H. Degen, and J. Abel. 2000. Regulation of prostaglandin endoperoxide H synthase-2 induction by dioxin in rat hepatocytes: Possible c-Src-mediated pathway. *Carcinogenesis* 21:2267-74.

37. Simanainen, U. J.T. Tuomisto, J. Tuomisto, and M. Viluksela. 2003. Dose-response analysis of short-term effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin in three differentially susceptible rat lines. *Toxicology and Applied Pharmacology* 187:128-36.

38. Senft, A.P., T.P. Dalton, D.W. Nebert, M.B. Genter, R.J. Hutchinson, and H.G. Shertzer. 2002. Dioxin increases reactive oxygen production in mouse liver mitochondria. *Toxicology and Applied Pharmacology* 178:15-21.

39. Kern, P.A., R.B. Fishman, W. Song, A.D. Brown, and V. Fonseca. 2002. The effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on oxidative enzymes in adipocytes and liver. *Toxicology* 171:117-25.

40. Lakshman, M.R., S.J. Chirtel, L.L. Chambers, and P.J. Coutlakis. 1989. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on lipid synthesis and lipogenic enzymes in the rat. *The Journal of Pharmacology and Experimental Therapeutics* 248:62-6.

41. Lakshman, M.R., B.S. Campbell, S.J. Chirtel, and N. Ekarohita. 1988. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on de novo fatty acid and cholesterol synthesis in the rat. *Lipids* 23:904-6.

42. Cantoni, L., A. Graziani, M. Rizzardini, and M.C. Saletti. 1986. Porphyrinogenic effect of hexachlorobenzene and 2,3,7,8-tetrachlorodibenzo-para-dioxin: Is an inhibitor involved in uroporphyrinogen decarboxylase inactivation? *IARC Scientific Publications* 77:449-56.

43. Goldstein, J.A., P. Hickman, and D.L. Jue. 1974. Experimental hepatic porphyria induced by polychlorinated biphenyls. *Toxicology and Applied Pharmacology* 27:437-48.

44. Bleiberg, J., M. Wallen, R. Brodkin, and I.L. Applebaum. 1964. Industrially acquired porphyria. *Archives of Dermatology* 89:793-7.

45. Lucier, G.W., R.C. Rumbaugh, Z. McCoy, R. Hass, D. Harvan, and P. Albro. 1986. Ingestion of soil contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) alters hepatic enzyme activities in rats. *Fundamental and Applied Toxicology* 6:364-71.

46. Calvert, G.M., R.W. Hornung, M.H. Sweeney, M.A. Fingerhut, and W.E. Halperin. 1992. Hepatic and gastrointestinal effects in an occupational cohort exposed to 2,3,7,8-tetrachlorodibenzo-para-dioxin. *The Journal of the American Medical Association* 267:2209-14.

47. Hoffman, R.E., P.A. Stehr-Green, K.B. Webb, R.G. Evans, A.P. Knutsen, W.F. Schramm, J.L. Staake, B.B. Gibson, and K.K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *The Journal of the American Medical Association* 255:2031-8.

48. Ideo, G., G. Bellati, A. Bellobuono, P. Mocarelli, A. Marocchi, and P. Brambilla. 1982. Increased urinary D-glucaric acid excretion by children living in an area polluted with tetrachlorodibenzoparadioxin (TCDD). *Clinica Chimica Acta; International Journal of Clinical Chemistry* 120:273-83.

49. Ideo, G., G. Bellati, A. Bellobuono, and L. Bissanti. 1985. Urinary d-glucaric acid excretion in the Seveso area, polluted by tetrachloro-dibenzo-p-dioxin (TCDD): Five years of experience. *Environmental Health Perspectives* 60:51-7.

50. U.S. Centers for Disease Control. 1988. Health status of Vietnam veterans. II. Physical Health. The Centers for Disease Control Vietnam Experience Study. *The Journal of the American Medical Association* 259:2708-14.

51. Kancir, C.B., C. Andersen, and A.S. Olesen. 1988. Marked hypocalcemia in a fatal poisoning with chlorinated phenoxy acid derivatives. *Clinical Toxicology* 26:257-64.

52. Meulenbelt, J., J.H. Zwaveling, P. van Zoonen, and N.C. Notermans. 1988. Acute MCPP intoxication: Report of two cases. *Human Toxicology* 7:289-92.

53. Geusau, A., K. Abraham, K. Geissler, M.O. Sator, G. Stingl, and E. Tschachler. 2001. Severe 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) intoxication: Clinical and laboratory effects. *Environmental Health Perspectives* 109:865-9.

54. Assennato, G., D. Cervino, E.A. Emmett, G. Longo, and F. Merlo. 1989. Follow-up of subjects who developed chloracne following TCDD exposure at Seveso. *American Journal of Industrial Medicine* 16:119-25.

55. Caramaschi, F., G. del Corno, C. Favaretti, S.E. Giambelluca, E. Montesarchio, and G.M. Fara. 1981. Chloracne following environmental contamination by TCDD in Seveso, Italy. *International Journal of Epidemiology* 10:135-43.

56. Mocarelli, P., A. Marocchi, P. Brambilla, P. Gerthoux, C. Beretta, L. Colombo, M. Bertona, C. Sarto, P. Tramacere, A. Mondonico, C. Crespi, S. Signorini, and R. Brivio. 1992. Human data derived from the Seveso accident—relevance for human risk assessment. *Toxic Substances Journal* 12:151-73.

57. Bertazzi, P.A., D. Consonni, S. Bachetti, M. Rubagotti, A. Baccarelli, C. Zocchetti, and A.C. Pesatori. 2001. Health effects of dioxin exposure: A 20-year mortality study. *American Journal of Epidemiology* 153:1031-44.

58. May, G. 1982. Tetrachlorodibenzodioxin: A survey of subjects ten years after exposure. *British Journal of Industrial Medicine* 39:128-35.

59. Mocarelli, P., A. Marocchi, P. Brambilla, P. Gerthoux, D.S. Young, and N. Mantel. 1986. Clinical laboratory manifestations of exposure to dioxin in children. A six-year study of the effects of an environmental disaster near Seveso, Italy. *The Journal of the American Medical Association* 256:2687-95.

60. Webb, K.B., R.G. Evans, A.P. Knutsen, S.T. Roodman, D.W. Roberts, W.F. Schramm, B.B. Gibson, J.S. Andrews, Jr., L.L. Needham, and D.G. Patterson. 1989. Medical evaluation of subjects with known body levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 28:183-93.

61. Webb, K., R.G. Evans, P. Stehr, and S.M. Ayres. 1987. Pilot study on health effects of environmental 2,3,7,8-TCDD in Missouri. *American Journal of Industrial Medicine* 11:685-91.

62. Bond, G.G., M.G. Ott, F.E. Brenner, and R.R. Cook. 1983. Medical and morbidity surveillance findings among employees potentially exposed to TCDD. *British Journal of Industrial Medicine* 40:318-24.

63. Calvert, G.M., K.K. Willie, M.H. Sweeney, M.A. Fingerhut, and W.E. Halperin. 1996. Evaluation of serum lipid concentrations among U.S. workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Archives of Environmental Health* 51:100-7.

64. Moses, M., R. Lilis, K.D. Crow, J. Thornton, A. Fischbein, H.A. Anderson, and I.J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *American Journal of Industrial Medicine* 5:161-82.

65. Neuberger, M., C. Rappe, S. Bergek, H. Cai, M. Hansson, R. Jager, M. Kundi, C.K. Lim, H. Wingfors, and A.G. Smith. 1999. Persistent health effects of dioxin contamination in herbicide production. *Environmental Research* 81:206-14.

66. Pazderova-Vejlupkova, J., E. Lukas, M. Nemcova, J. Pickova, and L. Jirasek. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Archives of Environmental Health* 36:5-11.

67. Pelclova, D., Z. Fenclova, Z. Dlaskova, P. Urban, E. Lukas, B. Prochazka, C. Rappe, J. Preiss, A. Kocan, and J. Vejlupkova. 2001. Biochemical, neuropsychological, and neurological abnormalities following 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure. *Archives of Environmental Health* 56:493-500.

68. Ott, M.G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.

69. Ott, M.G., and A. Zober. 1996. Morbidity study of extruder personnel with potential exposure to brominated dioxins and furans. II. Results of clinical laboratory studies. *Occupational and Environmental Medicine* 53:844-6.

70. Zober, A., M.G. Ott, and P. Messerer. 1994. Morbidity follow up study of BASF employees exposed to 2,3,7, 8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

71. Pelclova, D., Z. Fenclova, J. Preiss, B. Prochazka, J. Spacil, Z. Dubska, B. Okrouhlik, E. Lukas, and P. Urban. 2002. Lipid metabolism and neuropsychological follow-up study of workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *International Archives of Occupational and Environmental Health* 75(Suppl 1):60-6.

72. Hu, S.W., T.J. Cheng, G.P. ChangChien, and C.C. Chan. 2003. Association between dioxins/furans exposures and incinerator workers' hepatic function and blood lipids. *Journal of Occupational and Environmental Medicine* 45:601-8.

73. Takata, T. 2003. Survey on the health effects of chronic exposure to dioxins and its accumulation on workers of a municipal solid waste incinerator, rural part of Osaka Prefecture, and the results of extended survey afterwards. *Industrial Health* 41:189-96.

74. Kitamura, K., Y. Kikuchi, S. Watanabe, G. Waechter, H. Sakurai, and T. Takada. 2000. Health effects of chronic exposure to polychlorinated dibenzo-P-dioxins (PCDD), dibenzofurans (PCDF) and coplanar PCB (Co-PCB) of municipal waste incinerator workers. *Journal of Epidemiology/Japan Epidemiological Association* 10:262-70.

75. Von Benner, A., L. Edler, K. Mayer, and A. Zober. 1994. 'Dioxin' investigation program of the chemical industry professional association. *Arbeitsmedizin Sozialmedizin Praventivmedizin* 29:11-6.

76. Michalek, J.E., N.S. Ketchum, and F.Z. Akhtar. 1998. Postservice mortality of U.S. Air Force veterans occupationally exposed to herbicides in Vietnam: 15-year follow-up. *American Journal of Epidemiology* 148:786-92.

77. Michalek, J.E., N.S. Ketchum, and M.P. Longnecker. 2001. Serum dioxin and hepatic abnormalities in veterans of Operation Ranch Hand. *Annals of Epidemiology* 11:304-11.

78. Wolfe, W.H., J.E. Michalek, J.C. Miner, A. Rahe, J. Silva, W.F. Thomas, W.D. Grubbs, M.B. Lustik, T.G. Karrison, R.H. Roegner, and D.E. Williams. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. I. Physical health. *The Journal of the American Medical Association* 264:1824-31.

79. Tamburro, C.H. 1992. Chronic liver injury in phenoxy herbicide-exposed Vietnam veterans. *Environmental Research* 59:175-88.

80. Lathrop, G.D., S.G. Machado, T.G. Karrison, W.D. Grubbs, W.F. Thomas, W.H. Wolfe, J.E. Michalek, J.C. Miner, and M.R. Peterson. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline morbidity study results. NTIS: AD A 138 340. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

81. Michalek, J.E., B.R. Burnham, H.E. Marden, Jr., J.N. Robinson, V.V. Elequin, J.C. Miner, R.W. Ogershok, W.K. Sneddon, W.D. Grubbs, B.C. Cooper, R.G. Land, V.K. Rocconi, M.E. Yeager, D.E. Williams, and M.E.B. Owens. 2000. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1997 follow-up examination results. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

82. Institute of Medicine. 1994. Health effects of herbicides used in Vietnam. National Academy Press: Washington, DC.

83. Pesatori, A.C., D. Consonni, S. Bachetti, C. Zocchetti, M. Bonzini, A. Baccarelli, and P.A. Bertazzi. 2003. Short- and long-term morbidity and mortality in the population exposed to dioxin after the "Seveso Accident." *Industrial Health* 41:127-38.

84. Hooiveld, M., D.J. Heederik, M. Kogevinas, P. Boffetta, L.L. Needham, D.G. Patterson, Jr., and H.B. Bueno-de-Mesquita. 1998. Second follow-up of a Dutch cohort occupationally exposed to phenoxy herbicides, chlorophenols, and contaminants. *American Journal of Epidemiology* 147:891-901.

85. Flesch-Janys, D., K. Steindorf, P. Gurn, and H. Becher. 1998. Estimation of the cumulated exposure to polychlorinated dibenzo-p-dioxins/furans and standardized mortality ratio analysis of cancer mortality by dose in an occupationally exposed cohort. *Environmental Health Perspectives* 106(Suppl 2):655-62.

86. Kogevinas, M., H. Becher, T. Benn, P.A. Bertazzi, P. Boffetta, H.B. Bueno-de-Mesquita, D. Coggon, D. Colin, D. Flesch-Janys, M. Fingerhut, L. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, N. Pearce, and R. Saracci. 1997. Cancer mortality in workers exposed to phenoxy herbicides, chlorophenols, and dioxins. An expanded and updated international cohort study. *American Journal of Epidemiology* 145:1061-75.

87. Ott, M.G., and A. Zober. 1996. Cause specific mortality and cancer incidence among employees exposed to 2,3,7,8-TCDD after a 1953 reactor accident. *Occupational and Environmental Medicine* 53:606-12.

88. Ramlow, J.M., N.W. Spadacene, S.R. Hoag, B.A. Stafford, J.B. Cartmill, and P.J. Lerner. 1996. Mortality in a cohort of pentachlorophenol manufacturing workers, 1940-1989. *American Journal of Industrial Medicine* 30:180-94.

89. Vena, J., P. Boffetta, H. Becher, T. Benn, H.B. Bueno-de-Mesquita, D. Coggon, D. Colin, D. Flesch-Janys, L. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, N. Pearce, A.C. Pesatori, R. Saracci, K. Steenland, and M. Kogevinas. 1998. Exposure to dioxin and nonneoplastic mortality in the expanded IARC international cohort study of phenoxy herbicide and chlorophenol production workers and sprayers. *Environmental Health Perspectives* 106(Suppl 2):645-53.

90. Fett, M.J., J.R. Nairn, D.M. Cobbin, and M.A. Adena. 1987. Mortality among Australian conscripts of the Vietnam conflict era. II. Causes of death. *American Journal of Epidemiology* 125:878-84.

91. Thomas, T.L., and H.K. Kang. 1990. Mortality and morbidity among Army Chemical Corps Vietnam veterans: A preliminary report. *American Journal of Industrial Medicine* 18:665-73.

92. Institute of Medicine. 1997. Veterans and Agent Orange: Update 1996. National Academy Press: Washington, DC.

93. Institute of Medicine. 1999. Veterans and Agent Orange: Update 1998. National Academy Press: Washington, DC.

94. Institute of Medicine. 2001. Veterans and Agent Orange: Update 2000. National Academy Press: Washington, DC.

95. Garrow, J.S., and J. Webster. 1985. Quetelet's index (W/H^2) as a measure of fatness. *International Journal of Obesity* 9:147-53.

96. Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L. R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

97. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57:369-78.

98. Zimmerman, H.J. 1999. Hepatotoxicity: The Adverse Effects of Drugs and Other Chemicals on the Liver. 2nd ed. Lippincott Williams & Wilkins: Baltimore, MD.

99. Zakim, D., and T.D. Boyer. 2002. Hepatology: A Textbook of Liver Disease 4th ed. W.B. Saunders Company: Philadelphia, PA.

100. Centers for Disease Control and Prevention. 1998. Recommendations for prevention and control of Hepatitis C Virus (HCV) infection and HCV-related chronic disease. *Morbidity and Mortality Weekly Report* 47 (RR-19):1-39.

101. El-Serag, H.B., and A.C. Mason. 1999. Rising incidence of hepatocellular carcinoma in the United States. *The New England Journal of Medicine* 340(10):745-50.

102. Burt, A.D., R.N.T. Macsween, T. Peters, and K.J. Simpson. 1991. Nonalcoholic fatty liver: Causes and complications. In: Oxford Textbook of Clinical Hepatology. Vol. 2, 1st ed. N. McIntyre, J. Benhamou, J. Bircher, M. Rizzetto, and J. Rodes, eds. Oxford University Press: New York, NY.

103. Kim, W.R., R.S. Brown, Jr., N.A. Terrault, and H. El-Serag. 2002. Burden of liver disease in the United States: Summary of a workshop. *Hepatology* 36:227-42.

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14 DERMATOLOGY ASSESSMENT

14.1 INTRODUCTION

14.1.1 Background

The dermatology assessment of participants in the Air Force Health Study (AFHS) included the occurrence of self-reported acne and physical examination. Of particular interest was the detection of chloracne after exposure to herbicides and dioxin. Chloracne is recognized as a consequence of exposure to high levels of chlorophenols. Chloracne, however, usually appears after a short interval of exposure to dioxin, without a long latency period, and usually persists for 2 to 3 years. Therefore, primary lesions were not expected to be noted at the 2002 physical examination. No biopsies to confirm the diagnosis of chloracne were deemed necessary by the examining dermatologists. Consequently, analysis was limited to secondary lesions, such as scarring, hyperpigmentation, and depigmentation. If secondary lesions had been observed, chloracne might be suggested if the lesions had been found in the typical distribution areas of chloracne. In addition, the occurrence, duration, and location of acne were studied because of the absence of chloracne in AFHS veterans.

The analysis in this chapter is based on the participant-reported lifetime occurrence of acne, the occurrence of acne in relation to time of duty, and the location of acne (e.g., temples, eyes, ears). Acneiform lesions, acneiform scars, comedones, inclusion cysts, depigmentation, and hyperpigmentation, as found by a dermatologist upon a physical examination of the skin, also were studied to investigate whether there were any secondary lesions that could be suggestive of chloracne.

14.1.1.1   Organs/Diseases

Chloracne is a chronic acneiform eruption with a highly specific cutaneous distribution that was first described by Von Bettman in 1897 as an occupational disease in German industrial workers. It was not until 1957 that it became recognizable as a very specific, but not sensitive, consequence of exposure to high levels of chlorophenols (1, 2). Chronic conditions associated with severe chloracne include actinic elastosis, acne scars, and hypertrichosis (3, 4); epidermoid inclusion cysts seen in biopsy specimens are considered pathognomonic (5). The occurrence and severity of chloracne appear to be dose-related, but may depend on other factors, such as the route of administration, age, genetic predisposition, and the presence of acne vulgaris and other dermatoses (3, 6, 7). Literature reviews have described the unique clinical manifestations of chloracne (8-14), and case studies of humans exposed to dioxins have reported dermatologic effects (e.g., chloracne) described earlier in animals (10, 15-21). In one study, patients with chloracne following an industrial accident showed high dioxin serum concentrations, but chloracne did not appear to be a sensitive symptom of dioxin contamination, with some indication of a role of individual susceptibility (22).

14.1.1.2   Toxicology

Some of the first studies assayed the effects of chloracnegenic compounds using the rabbit's ear as a model (23, 24). Other experiments for such effects on hairless mice produced a variety of histopathologic changes, including hyperkeratotic changes in the sebaceous follicle with plugging of the orifice, hyperkeratinization of the stratum corneum, and keratin cyst formation (25-30). Chloracne and other dermal effects as a consequence of dioxin exposure also have been observed in monkeys (31), rats (32),

and domestic animals (33, 34); however, not all animal species appear sensitive to the chloracnegenic effects of dioxin (35).

A genetic basis for the dermal responses to dioxin has been described in selected laboratory animals. In one series of experiments, investigators found strain-specific differences in the cutaneous reactions of haired and hairless mice to the topical application of dioxin (36). The involvement of sebaceous glands and increased transglutamase activity were noted in both strains, while epidermal proliferation and hyperkeratinization occurred in the responsive (haired) strain only. Furthermore, in a subsequent study at the same laboratory, these dioxin-induced dermal changes were associated with an increased density of Langerhans' cells in mouse skin unique to the responsive strain (37). These and other studies (26, 38, 39) suggest that these strain-specific responses are determined genetically, and evidence exists that they may be mediated by the aryl hydrocarbon (Ah) receptor (27, 40, 41).

14.1.1.3   Epidemiology

Several small case series evaluated dioxin exposure and the development of chloracne (42) and chloracne and serum dioxin levels (43). Other skin conditions sporadically reported in relation to dioxin exposure include red and irritated eyes, hyperpigmentation, actinic elastosis, Peyronie's disease, and porphyria cutanea tarda (14, 44, 45). Studies of dioxin-related chloracne included populations exposed to dioxin through environmental contamination (46-61), occupation (4, 7, 44, 62-68), and during service in Southeast Asia (SEA) (89-98).

One of the most severe human exposures to dioxin occurred consequent to the industrial explosion in Seveso, Italy, in 1976 (22, 46, 48-52, 55, 60, 61). In the area closest to the explosion, a median serum dioxin level of 443 parts per trillion (ppt) was measured immediately after the accident among residents older than 13 years (n=177); in areas farther away from the accident site, median serum dioxin levels were found to be 87 ppt in a lower-exposed area (n=54) and 15 ppt in the lowest-exposed area (n=17) (60). A total of 193 cases of chloracne was observed, including 86 females and 107 males. Eighty-eight percent of the cases were children under 15 years of age; only seven cases were found among adults older than 20 years of age (46). The acnegenic toxic action of dioxin exposure on the skin was thought to last about 2 years (50). The last chloracne cases in the Seveso population were detected in 1978 (50), and all but one case had clinically recovered by 1983 (46). No cases of chloracne were reported among 36 workers exposed to dioxins during the cleanup of a chemical spill in Seveso, Italy (62). In a residential population exposed to dioxins after waste byproducts contaminated with dioxin were mixed with oils and widely sprayed for dust control in residential areas in eastern Missouri, no cases of chloracne were observed (54, 56, 57).

Chloracne has been associated with occupational dioxin exposure in several cohorts, including workers in the United States (4, 64-66, 70, 71, 75, 80), Germany (63, 79, 81), Austria (76-78), China (68, 69), Czech Republic (42), Russia (43, 88), United Kingdom (86), and Italy (62). In a National Institute of Occupational Safety and Health study of 281 workers exposed to chemicals contaminated with dioxin, chloracne was associated with the highest serum dioxin levels (87). In a study of 2,192 Dow Chemical workers potentially exposed to dioxin between 1940 and 1982, almost 16 percent of the workers were found to have chloracne (64-66, 70, 99), and chloracne incidence was positively associated with measures of intensity and cumulative exposure to dioxins (64). Among 73 male employees in a U.S. herbicide production plant, chloracne was found in 18 percent of the workers; however, chloracne was not substantially correlated with indicators of potential dioxin exposure, such as job location within the plant and duration of employment (80). In a 2,4,5-T production facility, clinical evidence of chloracne was found in 55.7 percent of 204 workers exposed to dioxin in a process accident, and no cases of chloracne were observed among 163 unexposed workers (4). Cases of chloracne were not observed among 482 persons potentially exposed to dioxins after an electrical transformer fire in Binghamton, New York (71).

Two small studies (63, 72) of occupationally exposed German chemical plant employees found serum dioxin levels moderately correlated to the occurrence of chloracne (63), and positively correlated with duration of chloracne (72). After a 1953 chemical accident at a BASF facility in Germany, 102 of 158 men exposed to dioxin developed chloracne within 1 year of the accident (83), and estimates of cumulative serum dioxin levels were found to correlate well with the severity of chloracne (79). In a German cohort of chemical workers in six plants, no association overall was reported between chloracne status and serum dioxin levels; however, some positive correlations were observed for several individual plants (82).

A study of nine production workers within a larger cohort found that those with a history of chloracne had significantly higher median serum dioxin levels (340 ppt) compared to workers without chloracne and known occupational exposure (18 ppt), as well as 17 external controls (16 ppt) (76).

Studies of Vietnam veterans generally have not found an association between dioxin exposure and the occurrence of self-reported chloracne, most likely because small numbers of Vietnam veterans were exposed to high levels of dioxin. Dermatology examinations do not appear to reveal any confirmed cases of chloracne (89-97). In one study (91), veterans who served in Vietnam had a higher prevalence of self-reported cutaneous disease compared with controls; however, the diagnosis was not clinically confirmed and the exposure indices were not validated. In the Vietnam Experience Study, the occurrence of dermatologic disorders found upon physical examination was similar in Vietnam and non-Vietnam veterans (90). In a study of Korean Vietnam veterans published in 2003, the frequency of chloracne was similar among Vietnam veterans compared to non-Vietnam veterans, and no trends were seen across semi-quantitative levels of Agent Orange exposure among Vietnam veterans (98). The AFHS is unique among studies that have examined for chloracne in Vietnam veterans because serial serum dioxin data have been incorporated into longitudinal analyses (92-97). At the 1987 AFHS follow-up examination, a higher prevalence of self-reported acne after service in SEA was found among Ranch Hand personnel as contrasted with Comparison subjects (92). No Ranch Hands or Comparison subjects, however, were diagnosed with chloracne based on dermatologic examination, and little evidence for a difference between the Ranch Hands and the Comparison group in the prevalence of other skin conditions was observed (92). Also, in a 1998 publication based on data collected on veterans participating in the AFHS, the risk of acne on the temples, eyes, or ears was not related to serum dioxin levels (96).

In the 1994 report published by the Institute of Medicine (IOM), the Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides concluded that there is sufficient evidence of an association between exposure to dioxin and chloracne (100). This conclusion remained unaltered in the 2002 IOM report (45); however, the committee added a notation in this report that chloracne would appear shortly after dioxin exposure and not after a long latency (45).

14.1.2   Summary of Previous Analyses of the Air Force Health Study

14.1.2.1   1982 Baseline Examination Summary Results

The 1982 baseline examination focused on the diagnosis of chloracne both in historical terms by a detailed questionnaire and in contemporary terms through a comprehensive clinical assessment. The questionnaire data did not demonstrate anatomic, prevalence, or onset-time patterns of acne in the Ranch Hand group that might support an inference of past chloracne, nor did the physical examination detect a case of chloracne. Fourteen biopsies from 11 participants also did not document a chloracne diagnosis, nor did the physical examination detect a case of chloracne. A dermatology index (a composite of the dependent variables comedones, acneiform lesions, acneiform scars, and inclusion cysts) was similar in the Ranch Hand and Comparison groups. No exposure index associations were noted in any occupational

category of the Ranch Hand group. The comprehensive dermatology assessment did not reveal evidence of past or current chloracne in the Ranch Hand group.

14.1.2.2   1985 Follow-up Examination Summary Results

Data from the 1985 follow-up examination participant questionnaire updated information gathered on acne through the 1982 baseline questionnaire, and the physical examination endpoints were similar to the 1982 baseline examination. Data on the occurrence, time, and location of acne were analyzed to assess the possible historical diagnosis of chloracne. No significant difference was observed between groups for reported occurrence or duration of acne.

For participants with acne after the start of the first qualifying tour of duty in SEA, the spatial eyeglass distribution of acne (suggesting chloracne) was observed to be similar for the Ranch Hand and Comparison groups, both for individual sites and the combination of acne on the temples, eyes, or ears. This analysis suggested that the occurrence of skin disease compatible with chloracne was not different in the two groups.

Analyses of the 1985 follow-up physical examination data, as with the baseline examination, placed primary emphasis on six dermatologic disorders: comedones, acneiform lesions, acneiform scars, inclusion cysts, depigmentation, and hyperpigmentation. The adjusted analyses showed no significant difference noted between groups for any variable. Exposure index analyses did not reveal a meaningful pattern of results suggesting a relation between skin disease and herbicide exposure.

Overall, the 1985 follow-up examination results paralleled the 1982 baseline examination findings. The 1985 follow-up examination detected more dermatologic abnormalities than those present at the baseline examination, and slightly more abnormalities were found in the Comparisons, but the contrasts of Ranch Hands and Comparisons were nonsignificant.

14.1.2.3   1987 Follow-up Examination Summary Results

With the exception of more Ranch Hands than Comparisons reporting acne during their lifetime, no significant group differences were detected. Subsequent analysis of the occurrence of acne indicated that, for participants with no history of acne before the start of the first SEA duty, a higher percentage of Ranch Hands than Comparisons reported the occurrence of acne after the start of the first SEA duty. The anatomic distribution of these lesions, however, did not suggest chloracne as a cause. No cases of chloracne were diagnosed in the physical examination. Analyses were conducted on historical occurrence and duration of acne, six dermatologic disorders, a composite variable of other disorders, and a dermatology index combining four disorders. All of these analyses found no significant group differences. The longitudinal analysis, based on the dermatology index, showed no significant differences between groups over time.

14.1.2.4   Serum Dioxin Analysis of 1987 Follow-up Examination Summary Results

For Ranch Hands who reported acne prior to the start of their first qualifying tour of duty in SEA, acne after the start of the first SEA duty increased as initial dioxin increased. Of the physical examination variables, only hyperpigmentation had a significant positive association with initial dioxin.

A significant positive association between 1987 dioxin and the occurrence of reported acne (lifetime) was seen for Ranch Hands who served in SEA during a later qualifying tour of duty. Further stratified analysis suggested that this association was related to acne after the start of the first SEA qualifying tour in Ranch Hands who had a history of acne prior to service in SEA. Lifetime acne was stratified further by

presence of acne prior to service in SEA ("pre-SEA acne" – yes or no), and the presence of acne after the beginning of service in SEA was analyzed separately for each pre-SEA acne stratum. These stratified analyses suggested that this significant positive association between lifetime acne and 1987 dioxin was related to acne after the start of the first SEA qualifying tour in Ranch Hands who had a history of acne prior to service in SEA. Several of the physical examination variables also had significant positive associations with 1987 dioxin levels for Ranch Hands who served in SEA during a later qualifying tour of duty.

No significant differences were found between the low and background dioxin categories or between the high and background categories for any of the variables. No cases of chloracne were identified, nor were there any dermatologic endpoints consistently related to the 1987 dioxin level. Also, the longitudinal analysis of the dermatology index showed no significant associations with dioxin. In summary, there was no consistent evidence in these data to suggest a dioxin association on the dermatologic system.

14.1.2.5   1992 Follow-up Examination Summary Results

In general, the dermatology variables showed no significant differences between Ranch Hands and Comparisons, except for a few significant increases in occurrence of acne for Ranch Hand enlisted groundcrew participants. The analyses of categorized dioxin also indicated a significantly lower occurrence of dermatology index abnormalities for Ranch Hands in the low and high dioxin categories combined than for Comparisons. The analysis of dermatology index exhibited a significant inverse association with 1987 dioxin.

In summary, there was no consistent evidence in these data to suggest an adverse dioxin association on the skin at doses received by U.S. military personnel in SEA.

14.1.2.6   1997 Follow-up Examination Summary Results

Dermatology endpoints were not analyzed statistically for the 1997 AFHS follow-up examination report.

14.1.3 Parameters for the 2002 Dermatology Assessment

14.1.3.1   Dependent Variables

The dermatology assessment was based on physical examination data and information regarding acne, as obtained in a face-to-face interview with the participant.

14.1.3.1.1 Questionnaire Variables

During the health interview conducted as part of the questionnaire, each study participant was asked about occurrences of acne on the face since the date of the last health interview. This information was used to update data gathered through the AFHS 1997 follow-up examination. Information regarding the date and location of each acne occurrence also was collected. In most other clinical areas of the AFHS, data obtained from the health interview underwent verification by requesting medical records from the participants' physicians. It was expected that the majority of participants who reported acne, however, did not visit a physician for the acne. Consequently, the analysis of acne was based on participant-reported occurrences. The analyses performed in this chapter were based on the 1,951 participants who attended the 2002 follow-up examination.

The variables defined below were constructed from the acne data and analyzed in the dermatology assessment. The following four-cell diagram is used to aid in determining which subsets of participants were used in the analysis and were contrasted with each other.

	Post-SEA Acne	
Pre-SEA Acne	Yes	No
Yes	Cell 1	Cell 2
No	Cell 3	Cell 4

The sample size in each of these four cells is presented below:

	Post-SEA Acne	
Pre-SEA Acne	Yes	No
Yes	n=264	n=400
No	n=180	n=1,106

- Acne (lifetime):
  - Yes: at least one reported occurrence of acne (cells 1, 2, and 3)
  - No: no reported occurrences of acne (cell 4).
- Post-SEA Acne
  - Yes: at least one occurrence of acne that ended after the start of the participant's first qualifying tour of duty in SEA (cells 1 and 3)
  - No: all occurrences of acne ended before the start of the participant's first qualifying tour of duty in SEA (cell 2) or no reported occurrences of acne (cell 4).

Acne after the start of the first SEA duty (post-SEA acne) was further analyzed by examining if the occurrence of acne after duty in SEA may have been affected by whether the participant had acne prior to the start of his first qualifying tour of duty in SEA (pre-SEA acne). In particular, post-SEA acne was analyzed separately for two subsets of participants: (1) participants who had no acne prior to the start of their first qualifying tour of duty in SEA (no pre-SEA acne), and (2) participants who had at least one occurrence of acne prior to the start of their first qualifying tour of duty in SEA (with pre-SEA acne). That is,

- Post-SEA Acne (no pre-SEA acne)
  - Yes: first occurrence of acne began after the start of the participant's first qualifying tour of duty in SEA (cell 3)
  - No: no reported occurrences of acne (cell 4)

and

- Post-SEA Acne (with pre-SEA acne)
  - Yes: first occurrence of acne began before the start of the participant's first qualifying tour of duty in SEA and last occurrence of acne ended after the start of the participant's first qualifying tour of duty in SEA (cell 1)
  - No: all occurrences of acne ended prior to the start of the first duty in SEA (cell 2).

Location and duration of post-SEA acne were analyzed twice. Post-SEA acne, however, may occur with or without the presence of pre-SEA acne. One analysis included participants who had all their

occurrences of acne after the start of their first qualifying tour of duty in SEA (post-SEA acne, but no pre-SEA acne – cell 3) and thus may be a result of herbicide exposure. The second analysis included any participants who had an occurrence of acne after the start of their first qualifying tour of duty in SEA, regardless of whether they had pre-SEA acne (post-SEA acne, cells 1 and 3). Acne for this subset of participants may have been the result of herbicide exposure, but their post-SEA acne may have also been related to the presence of acne before their qualifying tour of duty.

Questions regarding the presence of acne emphasized acne on the temples, eyes, or ears, as acne on these locations may have been related to chloracne. Participant medical records were reviewed to determine if acne had been observed on the periumbilical or scrotal regions, but no occurrences in these regions were observed.

Location of acne was tabulated as follows:

- Temples
- Eyes (or eyelids)
- Ears
- Temples and eyes (or eyelids)
- Temples and ears
- Eyes (or eyelids) and ears
- Temples, eyes (or eyelids), and ears
- Other sites.

Note: If an individual had multiple-site involvement for one or more of the specified sites and for the category "other sites," then the specified site(s) category was assigned.

Total duration of acne was determined by adding the duration of each reported occurrence of acne from all AFHS questionnaires.

14.1.3.1.2 Physical Examination Variables

Six dermatologic conditions noted at the physical examination and a composite dermatologic index were analyzed. The following conditions were reported: acneiform lesions, acneiform scars, comedones, inclusion cysts, depigmentation, and hyperpigmentation of the skin. Depigmentation and hyperpigmentation were defined as areas of skin that were less or more pigmented relative to the rest of the skin. The dermatology index was created by combining results from the examination for comedones, acneiform lesions, acneiform scars, and inclusion cysts. A participant was defined as abnormal for this dermatology index if any of these conditions was present and defined as normal if none was present. No participants were excluded for medical reasons from the analyses of these variables. Abnormalities relating to skin malignancies were discussed in Chapter 10, Neoplasia Assessment.

14.1.3.2   Covariates

The covariates age, race, and occupation were used in all adjusted statistical analyses. Presence of pre-SEA was used as a covariate for the physical examination variables and was defined as "yes" if at least one occurrence of acne began before the start of the participant's first qualifying tour of duty in SEA (cells 1 and 2) and "no" otherwise (cells 3 and 4).

14.1.4 Statistical Methods

Table 14-1 summarizes the statistical analysis performed for the 2002 dermatology assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, exclusions, and statistical methods. The second part of this table further describes the covariates. A covariate was used in its continuous form whenever possible for adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 14-1.

Table 14-1. Statistical Analysis for the Dermatology Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Acne (lifetime)	Q-SR	D	Yes No	(1)	None	U:LR,CS A:LR
Post-SEA Acne	Q-SR	D	Yes No	(1)	None	U:LR,CS A:LR
Post-SEA Acne (no pre-SEA acne)	Q-SR	D	Yes No	(1)	(a)	U:LR,CS A:LR
Post-SEA Acne (with pre-SEA acne)	Q-SR	D	Yes No	(1)	(b)	U:LR,CS A:LR
Location of Post-SEA Acne (excluding participants with pre-SEA acne)	Q-SR	D	Temples Eyes or eyelids Ears Other sites	(1)	(c)	U:Descriptive,LR,CS A:LR
Location of Post-SEA Acne (all post-SEA occurrences)	Q-SR	D	Temples Eyes or eyelids Ears Other sites	(1)	(d)	U:Descriptive,LR,CS A:LR
Duration of Post-SEA Acne (excluding participants with pre-SEA acne) (months)	Q-SR	C	--	(1)	(c)	U:GLM,TT
Duration of Post-SEA Acne (all post-SEA occurrences) (months)	Q-SR	C	--	(1)	(d)	U:GLM,TT
Acneiform Lesions	PE	D	Yes No	(2)	None	U:LR,CS A:LR
Acneiform Scars	PE	D	Yes No	(2)	None	U:LR,CS A:LR
Comedones	PE	D	Yes No	(2)	None	U:LR,CS A:LR
Depigmentation	PE	D	Yes No	(2)	None	U:LR,CS A:LR
Hyperpigmentation	PE	D	Yes No	(2)	None	U:LR,CS A:LR

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Inclusion Cysts	PE	D	Yes No	(2)	None	U:LR,CS A:LR
Dermatology Index	PE	D	Abnormal: >0 Normal: 0	(2)	None	U:LR,CS A:LR

[a]Covariates:

(1) age, race, military occupation.

(2) age, race, military occupation, presence of pre-SEA acne (i.e., at least one occurrence of acne that began before the start of the participant's first qualifying tour of duty in SEA).

[b]Exclusions:

(a) participants with a reported pre-SEA history of acne (i.e., at least one occurrence of acne that began before the start of the participant's first qualifying tour of duty in SEA).

(b) participants without a reported pre-SEA history of acne (i.e., either no reported acne or all occurrences of acne began after the start of the participant's first qualifying tour of duty in SEA).

(c) participants with a reported pre-SEA history of acne (i.e., at least one occurrence of acne that began before the start of the participant's first qualifying tour of duty in SEA) or no reported acne.

(d) participants with only a reported pre-SEA history of acne (i.e., all occurrences of acne ended before the start of the participant's first qualifying tour of duty in SEA) or no reported acne.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	C/D	Born ≥ 1942 Born < 1942
Race	MIL	D	Black Non-Black
Military Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Presence of Pre-SEA Acne	Q-SR	D	Yes No

Abbreviations

Data Source: MIL: Air Force military records
PE: 2002 physical examination
Q-SR: Health questionnaires (self-reported)

Data Form: D: Discrete form of dependent variable or covariate
C: Continuous form of dependent variable
C/D: Appropriate form for analysis (either continuous or discrete) of covariate

Statistical Analysis: U: Unadjusted analysis
A: Adjusted analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
GLM: General linear models analysis
LR: Logistic regression analysis
TT: Two-sample t-test

Four models were examined for each dependent variable given in Table 14-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for covariates. These covariates are given in Table 14-1. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. In an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-4, the median level of exposure to dioxin was highest for enlisted groundcrew, followed by enlisted flyers, then officers.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the Centers for Disease Control and Prevention (CDC) using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in ppt on a lipid weight basis (101). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2. A statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model to account for body mass index-related differences in elimination rate (102).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. Another category was examined by combining the low and high Ranch Hand categories. This combination is referred to in the tables as the "low plus high Ranch Hand" category. These five categories—Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the four Ranch Hand categories and the dependent variable in the Comparison category was examined. As in Model 2, a statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables. One Ranch Hand without a dioxin measure was excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The term "unadjusted" was used in the text and tables as follows: Models 1 and 4 did not adjust for any covariates. Models 2 and 3 adjusted only for body mass index at the time of the blood measurement for dioxin. The term "adjusted" was used in the text and tables as follows: Models 1 and 4 adjusted for the covariates shown in Table 14-1 unless otherwise specified by a footnote to the table. Models 2 and 3 additionally adjusted only for body mass index at the time of the blood measurement for dioxin.

Table 14-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants that were excluded from analyses is given.

Table 14-2. Number of Participants with Missing Data for the Dermatology Assessment

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Time Reference Relative to SEA (pre-SEA or post-SEA)	DEP/EXC	0	1	0	0	0	1
Location of Post-SEA Acne	DEP	3	3	2	3	3	3
Duration of Post-SEA Acne	DEP	3	8	2	3	3	8
Presence of Pre-SEA Acne	COV	0	1	0	0	0	1

[a]777 Ranch Hands and 1,174 Comparisons for group.
[b]424 Ranch Hands for initial dioxin; 776 Ranch Hands for 1987 dioxin.
[c]776 Ranch Hands and 1,174 Comparisons for categorized dioxin.

Note: DEP = Dependent variable.
COV = Covariate.
EXC = Exclusion.

14.2 RESULTS

14.2.1 Dependent Variable-covariate Associations

The dermatology dependent variables were tested for associations with each of the covariates used in the adjusted analyses. The complete results are presented in Appendix F, Table F-6. These associations were pairwise between the dependent variable and the covariate and were not adjusted for any other covariates. A brief summary of the pattern of significant ($p \leq 0.05$) dependent variable-covariate associations is described in the following paragraphs.

Younger participants reported acne at some point in their lifetimes and acne after service in SEA more often than older participants. Younger participants had more acneiform lesions and acneiform scars than older participants. A greater prevalence of comedones and hyperpigmentation was found among older participants than among younger participants.

For participants who reported acne after service in SEA but not prior to service in SEA, Black participants reported acne more often than non-Black participants. On average, non-Black participants reported a longer duration of acne after the start of the first SEA duty than Black participants. Black participants

had more hyperpigmentation than non-Black participants. Non-Black participants had more abnormalities on the dermatology index than Black participants.

Enlisted groundcrew reported more acne after service in SEA than enlisted flyers, and enlisted flyers reported more acne after service in SEA than officers. Enlisted personnel had more acneiform lesions, comedones, and more abnormalities on the dermatology index than officers.

Participants who reported acne prior to service in SEA had more acneiform lesions, acneiform scars, comedones, inclusion cysts, and abnormalities on the dermatology index than participants who did not report acne prior to service in SEA.

14.2.2   Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 14-1. Dependent variables are grouped into two sections: (1) the questionnaire variables, derived from the questionnaire that was administered during the 2002 follow-up and previous AFHS examinations, and (2) variables obtained during the 2002 physical examination.

14.2.2.1   *Questionnaire Variables*

14.2.2.1.1 *Acne (Lifetime)*

The unadjusted and adjusted Model 1 analyses of self-reported acne over the lifetime of the participant revealed significant differences between all Ranch Hands and Comparisons (Table 14-3(a,b): Unadjusted Relative Risk [RR]=1.32, p=0.003; Adjusted RR=1.34, p=0.002). A greater percentage of Ranch Hands reported acne during their lifetime (47.5%) than did Comparisons (40.6%). After stratifying by military occupation, both the unadjusted and adjusted analyses showed a significant difference between Ranch Hand and Comparison enlisted groundcrew (Table 14-3(a,b): Unadjusted RR=1.64, p<0.001, Adjusted RR=1.61, p<0.001). A greater percentage of Ranch Hand enlisted groundcrew reported an occurrence of acne during their lifetime than Comparison enlisted groundcrew (52.8% versus 40.6%, respectively).

No significant relation between initial dioxin and lifetime occurrence of acne was seen in the unadjusted and adjusted Model 2 analyses (Table 14-3(c,d): p>0.05 for each analysis).

The unadjusted Model 3 analysis revealed three significant contrasts: Ranch Hands in the low dioxin category versus Comparisons (Table 14-3(e): Unadjusted RR=1.48, p=0.010), Ranch Hands in the high dioxin category versus Comparisons (Table 14-3(e): Unadjusted RR=1.42, p=0.019), and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 14-3(e): Unadjusted RR=1.45, p=0.001). After adjusting for covariates, two contrasts remained significant: Ranch Hands in the low dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 14-3(f): Adjusted RR=1.63, p=0.002; and Adjusted RR=1.45, p=0.002, respectively). The percentage of Ranch Hands in the low dioxin category who reported an occurrence of acne during their lifetime was 50.2 percent compared to 40.6 percent for Comparisons. In the low and high dioxin categories combined, 49.8 percent for Ranch Hands reported an occurrence of acne during their lifetime. All remaining unadjusted and adjusted Model 3 contrasts were not significant (Table 14-3(e,f): p>0.09 for each contrast).

All unadjusted and adjusted Model 4 analyses were nonsignificant (Table 14-3(g,h): p>0.33 for each analysis).

Table 14-3. Analysis of Acne (Lifetime)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*369 (47.5)*	*1.32 (1.10,1.59)*	*0.003***
	Comparison	*1,174*	*477 (40.6)*		
Officer	Ranch Hand	307	128 (41.7)	0.99 (0.74,1.32)	0.935
	Comparison	462	194 (42.0)		
Enlisted Flyer	Ranch Hand	133	63 (47.4)	1.51 (0.96,2.38)	0.073
	Comparison	185	69 (37.3)		
Enlisted Groundcrew	Ranch Hand	337	178 (52.8)	1.64 (1.24,2.16)	<0.001**
	Comparison	527	214 (40.6)		

**: Statistically significant (p-value≤0.010).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,951*	*1.34 (1.11,1.61)*	*0.002***
Officer	769	1.01 (0.75,1.36)	0.929
Enlisted Flyer	318	1.58 (1.00,2.50)	0.051
Enlisted Groundcrew	864	1.61 (1.22,2.14)	<0.001**

**: Statistically significant (p-value≤0.010).

(c) MODEL 2: RANCH HANDS − INITIAL DIOXIN − UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	71 (50.7)	0.95 (0.82,1.10)	0.466
Medium	143	75 (52.4)		
High	141	65 (46.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS − INITIAL DIOXIN − ADJUSTED

	Analysis Results for $\log_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
424	0.84 (0.71,1.00)	0.052

[a]Relative risk for a twofold increase in initial dioxin.

Table 14-3. Analysis of Acne (Lifetime) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	477 (40.6)		
Background RH	352	157 (44.6)	1.18 (0.92,1.50)	0.189
Low RH	211	106 (50.2)	1.48 (1.10,1.98)	0.010**
High RH	213	105 (49.3)	1.42 (1.06,1.91)	0.019*
Low plus High RH	424	211 (49.8)	1.45 (1.16,1.81)	0.001**

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,174		
Background RH	352	1.21 (0.94,1.56)	0.131
Low RH	211	1.63 (1.20,2.20)	0.002**
High RH	213	1.30 (0.95,1.76)	0.099
Low plus High RH	424	1.45 (1.15,1.83)	0.002**

[a]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 14-3. Analysis of Acne (Lifetime) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
Low	260	114 (43.8)	1.02 (0.93,1.11)	0.676
Medium	258	129 (50.0)		
High	258	125 (48.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
776	0.95 (0.86,1.05)	0.332

[a]Relative risk for a twofold increase in 1987 dioxin.

14.2.2.1.2 Post-SEA Acne

The unadjusted and adjusted Model 1 analyses of acne after service in SEA revealed significant differences between Ranch Hands and Comparisons for all participants (Table 14-4(a,b): Unadjusted RR=1.40, p=0.002; Adjusted RR=1.43, p=0.001). A greater percentage of Ranch Hands reported acne after service in SEA (26.4%) than did Comparisons (20.4%). After stratifying by military occupation, both the unadjusted and adjusted analyses showed a significant difference between Ranch Hand and Comparison enlisted groundcrew (Table 14-4(a,b): Unadjusted RR=1.62, p=0.001, Adjusted RR=1.60, p=0.003). A greater percentage of Ranch Hand enlisted groundcrew reported acne after service in SEA than Comparison enlisted groundcrew (35.0% versus 24.9%, respectively).

All unadjusted and adjusted Model 2 and 4 analyses of acne after service in SEA were nonsignificant (Table 14-4(c,d,g,h): p>0.16 for each analysis).

The unadjusted Model 3 analysis revealed significant differences in acne after service in SEA between Ranch Hands in the low dioxin category and Comparisons (Table 14-4(e): Unadjusted RR=1.47, p=0.023), between Ranch Hands in the high dioxin category and Comparisons (Table 14-4(e): Unadjusted RR=1.58, p=0.006), and between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 14-4(e): Unadjusted RR=1.53, p=0.001). After covariate adjustment, the contrast between Ranch Hands in the high dioxin category and Comparisons was no longer significant (Table 14-4(f): p=0.332). The contrast between Ranch Hands in the background dioxin category and Comparisons, however, became significant (Table 14-4(f): Adjusted RR=1.49, p=0.009). The difference between Ranch Hands in the low dioxin category and Comparisons, as well as the difference between Ranch Hands in the low and high dioxin categories combined and Comparisons, remained significant (Table 14-4(f): Adjusted RR=1.68, p=0.003; and Adjusted RR=1.41, p=0.011, respectively). The percentage of participants reporting acne after service in SEA was 23.9 percent for Ranch Hands in the background dioxin category, 27.5 percent for Ranch Hands in the low dioxin category, 29.1 percent for

Ranch Hands in the high dioxin category, 28.3 percent for Ranch Hands in the low and high dioxin categories combined, and 20.4 percent for Comparisons.

Table 14-4. Analysis of Post-SEA Acne

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*205 (26.4)*	*1.40 (1.13,1.73)*	*0.002***
	Comparison	*1,173*	*239 (20.4)*		
Officer	Ranch Hand	307	53 (17.3)	1.09 (0.74,1.61)	0.649
	Comparison	462	74 (16.0)		
Enlisted Flyer	Ranch Hand	133	34 (25.6)	1.53 (0.89,2.61)	0.125
	Comparison	185	34 (18.4)		
Enlisted Groundcrew	Ranch Hand	337	118 (35.0)	1.62 (1.21,2.19)	0.001**
	Comparison	526	131 (24.9)		

**: Statistically significant (p-value≤0.010).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,950*	*1.43 (1.15,1.78)*	*0.001***
Officer	769	1.13 (0.76,1.67)	0.538
Enlisted Flyer	318	1.59 (0.92,2.74)	0.096
Enlisted Groundcrew	863	1.60 (1.18,2.16)	0.003**

**: Statistically significant (p-value≤0.010).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	37 (26.4)	1.04 (0.89,1.22)	0.641
Medium	143	44 (30.8)		
High	141	39 (27.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 14-4. Analysis of Post-SEA Acne (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
424	0.92 (0.76,1.11)	0.382

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,173	239 (20.4)		
Background RH	352	84 (23.9)	1.25 (0.94,1.66)	0.129
Low RH	211	58 (27.5)	1.47 (1.06,2.06)	0.023*
High RH	213	62 (29.1)	1.58 (1.14,2.20)	0.006**
Low plus High RH	424	120 (28.3)	1.53 (1.18,1.97)	0.001**

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,173		
Background RH	352	1.49 (1.10,2.01)	0.009**
Low RH	211	1.68 (1.19,2.37)	0.003**
High RH	213	1.19 (0.84,1.68)	0.332
Low plus High RH	424	1.41 (1.08,1.83)	0.011*

[a]Relative risk and confidence interval relative to Comparisons.

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 14-4. Analysis of Post-SEA Acne (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
Low	260	63 (24.2)	1.06 (0.96,1.17)	0.251
Medium	258	64 (24.8)		
High	258	77 (29.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
776	0.92 (0.82,1.03)	0.161

[a]Relative risk for a twofold increase in 1987 dioxin.

14.2.2.1.3 Post-SEA Acne (No Pre-SEA Acne)

In an attempt to determine whether self-reported acne after service in SEA was related to the presence of acne prior to duty in SEA, two analyses were performed: reported acne after service in SEA without the presence of acne prior to service (this section), and reported acne after service in SEA along with the presence of acne prior to service in SEA (Section 14.2.2.1.4).

For participants who did not report acne prior to service in SEA, the unadjusted and adjusted Model 1 analyses of acne after service in SEA revealed a significant group difference between all Ranch Hands and Comparisons (Table 14-5(a,b): Unadjusted RR=1.70, p=0.001; Adjusted RR=1.78, p<0.001). After stratifying by military occupation, a significant difference in reported acne was observed between Ranch Hand and Comparison enlisted groundcrew in both the unadjusted and adjusted analyses (Table 14-5(a,b): Unadjusted RR=2.14, p<0.001; Adjusted RR=2.15, p<0.001). For all participants who did not report acne prior to service in SEA, Ranch Hands had a greater percentage of reported acne after service in SEA than Comparisons (18.0% versus 11.4%). Among enlisted groundcrew who did not report acne prior to service in SEA, Ranch Hands had a greater percentage of acne after service in SEA than Comparisons (26.3% versus 14.2%).

All unadjusted and adjusted Model 2 and 4 analyses of acne after service in SEA (for participants with no report of acne prior to service in SEA) were nonsignificant (Table 14-5(c,d,g,h): p>0.08 for each analysis).

The unadjusted Model 3 analysis revealed three significant contrasts for acne after service in SEA: Ranch Hands in the low dioxin category versus Comparisons (Table 14-5(e): Unadjusted RR=1.99, p=0.005), Ranch Hands in the high dioxin category versus Comparisons (Table 14-5(e): Unadjusted RR=2.19, p<0.001), and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 14-5(e): Unadjusted RR=2.09, p<0.001).

After adjusting for covariates, all four Model 3 contrasts were significant (Table 14-5(f): Adjusted RR=1.60, p=0.046 for Ranch Hands in the background dioxin category versus Comparisons; Adjusted RR=2.19, p=0.002 for Ranch Hands in the low dioxin category versus Comparisons; Adjusted RR=1.72, p=0.026 for Ranch Hands in the high dioxin category versus Comparisons; and Adjusted RR=1.93, p<0.001 for Ranch Hands in the low and high dioxin categories combined versus Comparisons). Among participants who did not report acne prior to service in SEA, the percentages of Ranch Hands reporting acne after service in SEA in the background dioxin category, low dioxin category, high dioxin category, and low and high dioxin categories combined were 14.1, 20.5, 22.1, and 21.3, respectively. Among Comparisons who did not report acne prior to service in SEA, 11.4 percent reported acne after service in SEA.

Table 14-5. Analysis of Post-SEA Acne (No Pre-SEA Acne)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*499*	*90 (18.0)*	*1.70 (1.24,2.34)*	*0.001***
	Comparison	*787*	*90 (11.4)*		
Officer	Ranch Hand	197	18 (9.1)	1.08 (0.57,2.03)	0.817
	Comparison	293	25 (8.5)		
Enlisted Flyer	Ranch Hand	85	15 (17.6)	1.91 (0.86,4.25)	0.112
	Comparison	129	13 (10.1)		
Enlisted Groundcrew	Ranch Hand	217	57 (26.3)	2.14 (1.41,3.27)	<0.001**
	Comparison	365	52 (14.2)		

**: Statistically significant (p-value≤0.010).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,286*	*1.78 (1.29,2.46)*	*<0.001***
Officer	490	1.11 (0.58,2.09)	0.759
Enlisted Flyer	214	1.98 (0.88,4.43)	0.098
Enlisted Groundcrew	582	2.15 (1.40,3.29)	<0.001**

**: Statistically significant (p-value≤0.010).

Table 14-5. Analysis of Post-SEA Acne (No Pre-SEA Acne) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a,b]**	**p-Value**
Low	85	16 (18.8)	1.06 (0.86,1.31)	0.596
Medium	90	22 (24.4)		
High	97	20 (20.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
272	0.88 (0.69,1.14)	0.331

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a,b]**	**p-Value**
Comparison	787	90 (11.4)		
Background RH	227	32 (14.1)	1.28 (0.83,1.98)	0.272
Low RH	132	27 (20.5)	1.99 (1.23,3.20)	0.005**
High RH	140	31 (22.1)	2.19 (1.39,3.46)	<0.001**
Low plus High RH	272	58 (21.3)	2.09 (1.45,3.01)	<0.001**

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 14-5. Analysis of Post-SEA Acne (No Pre-SEA Acne) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	787		
Background RH	227	1.60 (1.01,2.53)	0.046*
Low RH	132	2.19 (1.34,3.58)	0.002**
High RH	140	1.72 (1.07,2.78)	0.026*
Low plus High RH	272	1.93 (1.33,2.82)	<0.001**

[a]Relative risk and confidence interval relative to Comparisons.

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	170	24 (14.1)	1.13 (0.98,1.30)	0.086
Medium	157	28 (17.8)		
High	172	38 (22.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
499	0.98 (0.84,1.14)	0.763

[a]Relative risk for a twofold increase in 1987 dioxin.

14.2.2.1.4 Post-SEA Acne (with Pre-SEA Acne)

For participants who did report acne prior to service in SEA, all unadjusted and adjusted Model 1 through 4 analyses of reported acne after service in SEA were nonsignificant (Table 14-6(a-h): p>0.15 for each analysis). In comparing the results of this section and Section 14.2.2.1.3, it can be seen that the significant relations between either group or dioxin and the reporting of acne after service in SEA were confined to participants who did not report acne prior to service in SEA (see Tables 14-4 and 14-5).

Table 14-6. Analysis of Post-SEA Acne (with Pre-SEA Acne)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*278*	*115 (41.4)*	*1.12 (0.82,1.54)*	*0.473*
	Comparison	*386*	*149 (38.6)*		
Officer	Ranch Hand	110	35 (31.8)	1.14 (0.68,1.92)	0.615
	Comparison	169	49 (29.0)		
Enlisted Flyer	Ranch Hand	48	19 (39.6)	1.09 (0.49,2.41)	0.828
	Comparison	56	21 (37.5)		
Enlisted Groundcrew	Ranch Hand	120	61 (50.8)	1.07 (0.67,1.72)	0.770
	Comparison	161	79 (49.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*664*	*1.11 (0.80,1.53)*	*0.532*
Officer	279	1.18 (0.70,2.00)	0.534
Enlisted Flyer	104	1.16 (0.52,2.59)	0.713
Enlisted Groundcrew	281	1.03 (0.64,1.67)	0.888

(c) MODEL 2: RANCH HANDS − INITIAL DIOXIN − UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	55	21 (38.2)	1.10 (0.85,1.43)	0.472
Medium	53	22 (41.5)		
High	44	19 (43.2)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS − INITIAL DIOXIN − ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
152	1.10 (0.79,1.53)	0.557

[a]Relative risk for a twofold increase in initial dioxin.

Table 14-6. Analysis of Post-SEA Acne (with Pre-SEA Acne) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	386	149 (38.6)		
Background RH	125	52 (41.6)	1.18 (0.78,1.78)	0.440
Low RH	79	31 (39.2)	1.02 (0.62,1.67)	0.941
High RH	73	31 (42.5)	1.15 (0.69,1.91)	0.600
Low plus High RH	152	62 (40.8)	1.08 (0.73,1.58)	0.702

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	386		
Background RH	125	1.36 (0.89,2.10)	0.159
Low RH	79	1.17 (0.70,1.97)	0.549
High RH	73	0.76 (0.44,1.30)	0.311
Low plus High RH	152	0.95 (0.64,1.42)	0.800

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	90	39 (43.3)	1.02 (0.87,1.19)	0.802
Medium	101	36 (35.6)		
High	86	39 (45.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 14-6. Analysis of Post-SEA Acne (with Pre-SEA Acne) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
277	0.89 (0.74,1.07)	0.222

[a]Relative risk for a twofold increase in 1987 dioxin.

14.2.2.1.5 Location of Post-SEA Acne (Excluding Participants with Pre-SEA Acne)

The number of participants who reported acne after service in SEA is presented by location in Table 14-7. This table includes data on those participants who reported acne only after service in SEA.

Table 14-7. Location of Post-SEA Acne (Excluding Participants with Pre-SEA Acne)

	Group Sample Size	
Location	**Ranch Hand**	**Comparison**
Temples Only	11	14
Eyes (or Eyelids) Only	1	2
Ears Only	2	5
Temples and Eyes (or Eyelids)	3	0
Temples and Ears	2	2
Eyes (or Eyelids) and Ears	2	1
Temples, Eyes (or Eyelids), and Ears	5	2
Other Sites	62	63
Total	88	89

Location	**Initial Dioxin Sample Size**	**1987 Dioxin Sample Size**
Temples Only	7	11
Eyes (or Eyelids) Only	1	1
Ears Only	2	2
Temples and Eyes (or Eyelids)	2	3
Temples and Ears	1	2
Eyes (or Eyelids) and Ears	1	2
Temples, Eyes (or Eyelids), and Ears	3	5
Other Sites	39	62
Total	56	88

		Dioxin Category			
Location	**Comparison**	**Background Ranch Hand**	**Low Ranch Hand**	**High Ranch Hand**	**Low plus High Ranch Hand**
Temples Only	14	4	4	3	7
Eyes (or Eyelids) Only	2	0	0	1	1
Ears Only	5	0	2	0	2
Temples and Eyes (or Eyelids)	0	1	1	1	2
Temples and Ears	2	1	0	1	1
Eyes (or Eyelids) and Ears	1	1	0	1	1
Temples, Eyes (or Eyelids), and Ears	2	2	0	3	3
Other Sites	63	23	19	20	39
Total	89	32	26	30	56

The percentage of participants who reported acne on the temples, eyes, or ears after service in SEA was compared to the percentage of participants who reported acne after service in SEA on other sites. This analysis was restricted to participants who reported acne only after service in SEA. The relation between this comparison and either group or dioxin is given in Table 14-8. No significant results were seen in the unadjusted and adjusted Model 1 through 4 analyses of location of acne after service in SEA, where participants who reported acne prior to service in SEA were excluded (Table 14-8(a-h): $p>0.13$ for each analysis).

Table 14-8. Analysis of Location of Post-SEA Acne – Temples, Eyes, or Ears vs. Other Sites (Excluding Participants with Pre-SEA Acne)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes to Post-SEA Acne on Temples, Eyes, or Ears	Unadjusted Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	*88*	*26 (29.5)*	*1.02 (0.53,1.94)*	*0.961*
	Comparison	*89*	*26 (29.2)*		
Officer	Ranch Hand	18	2 (11.1)	0.50 (0.09,2.93)	0.442
	Comparison	25	5 (20.0)		
Enlisted Flyer	Ranch Hand	14	4 (28.6)	0.40 (0.08,2.02)	0.268
	Comparison	12	6 (50.0)		
Enlisted Groundcrew	Ranch Hand	56	20 (35.7)	1.37 (0.61,3.09)	0.447
	Comparison	52	15 (28.8)		

Table 14-8. *Analysis of Location of Post-SEA Acne – Temples, Eyes, or Ears vs. Other Sites (Excluding Participants with Pre-SEA Acne) (Continued)*

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*177*	*0.94 (0.49,1.82)*	*0.859*
Officer	43	0.50 (0.09,2.94)	0.444
Enlisted Flyer	26	0.42 (0.08,2.13)	0.295
Enlisted Groundcrew	108	1.34 (0.59,3.03)	0.481

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes to Post-SEA Acne on Temples, Eyes, or Ears	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	16	3 (18.8)	1.37 (0.91,2.07)	0.135
Medium	20	6 (30.0)		
High	20	8 (40.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
56	1.32 (0.86,2.02)	0.196

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for military occupation because of the sparse number of Ranch Hands with only post-SEA acne on the temples, eyes, or ears.

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(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes to Post-SEA Acne on Temples, Eyes, or Ears	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	89	26 (29.2)		
Background RH	32	9 (28.1)	0.97 (0.39,2.40)	0.949
Low RH	26	7 (26.9)	0.92 (0.34,2.48)	0.866
High RH	30	10 (33.3)	1.20 (0.49,2.91)	0.693
Low plus High RH	56	17 (30.4)	1.06 (0.51,2.20)	0.880

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	89		
Background RH	32	1.08 (0.42,2.79)	0.867
Low RH	26	0.79 (0.28,2.18)	0.643
High RH	30	0.98 (0.39,2.47)	0.972
Low plus High RH	56	0.89 (0.42,1.89)	0.754

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes to Post-SEA Acne on Temples, Eyes, or Ears	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	24	8 (33.3)	1.13 (0.87,1.47)	0.361
Medium	27	5 (18.5)		
High	37	13 (35.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

n	Analysis Results for Log$_2$ (1987 Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
88	1.03 (0.78,1.37)	0.836

[a]Relative risk for a twofold increase in 1987 dioxin.

14.2.2.1.6 Location of Post-SEA Acne (All Post-SEA Occurrences)

The number of participants who reported acne after service in SEA is presented by location in Table 14-9. Participants who reported acne after service in SEA are included in this table, regardless of whether they reported acne prior to service in SEA.

Table 14-9. Location of Post-SEA Acne (All Post-SEA Occurrences)

Location	Group Sample Size	
	Ranch Hand	**Comparison**
Temples Only	28	37
Eyes (or Eyelids) Only	3	4
Ears Only	9	13
Temples and Eyes (or Eyelids)	5	2
Temples and Ears	13	16
Eyes (or Eyelids) and Ears	3	2
Temples, Eyes (or Eyelids), and Ears	13	8
Other Sites	128	154
Total	202	236

Location	Initial Dioxin Sample Size	1987 Dioxin Sample Size
Temples Only	16	28
Eyes (or Eyelids) Only	1	3
Ears Only	6	9
Temples and Eyes (or Eyelids)	2	5
Temples and Ears	7	13
Eyes (or Eyelids) and Ears	1	3
Temples, Eyes (or Eyelids), and Ears	9	13
Other Sites	76	128
Total	118	202

Location	Comparison	Dioxin Category			
		Background Ranch Hand	Low Ranch Hand	High Ranch Hand	Low plus High Ranch Hand
Temples Only	37	12	9	7	16
Eyes (or Eyelids) Only	4	2	0	1	1
Ears Only	13	3	4	2	6
Temples and Eyes (or Eyelids)	2	3	1	1	2
Temples and Ears	16	5	3	4	7
Eyes (or Eyelids) and Ears	2	2	0	1	1
Temples, Eyes (or Eyelids), and Ears	8	4	4	5	9
Other Sites	154	52	36	40	76
Total	236	83	57	61	118

The percentage of participants who reported acne on the temples, eyes, or ears after service in SEA was compared to the percentage of participants who reported acne after service in SEA on other sites. This analysis included all participants who reported acne after service in SEA regardless of whether they reported acne prior to service in SEA. The relation between this comparison and either group or dioxin is given in Table 14-10. The unadjusted and adjusted Model 1 through 4 analyses of location of reported acne after service in SEA revealed no significant results (Table 14-10(a-h): p>0.45 for each analysis).

Table 14-10. Analysis of Location of Post-SEA Acne – Temples, Eyes, or Ears vs. Other Sites (All Post-SEA Occurrences)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes to Post-SEA Acne on Temples, Eyes, or Ears	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*202*	*74 (36.6)*	*1.09 (0.73,1.61)*	*0.681*
	Comparison	*236*	*82 (34.7)*		
Officer	Ranch Hand	53	17 (32.1)	1.09 (0.51,2.35)	0.816
	Comparison	73	22 (30.1)		
Enlisted Flyer	Ranch Hand	33	13 (39.4)	0.69 (0.26,1.83)	0.458
	Comparison	33	16 (48.5)		
Enlisted Groundcrew	Ranch Hand	116	44 (37.9)	1.19 (0.71,2.01)	0.505
	Comparison	130	44 (33.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*438*	*1.07 (0.72,1.58)*	*0.752*
Officer	126	1.10 (0.51,2.36)	0.809
Enlisted Flyer	66	0.70 (0.26,1.85)	0.470
Enlisted Groundcrew	246	1.19 (0.70,2.01)	0.521

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Yes to Post-SEA Acne on Temples, Eyes, or Ears**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	37	13 (35.1)	1.05 (0.79,1.40)	0.736
Medium	42	15 (35.7)		
High	39	14 (35.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
118	1.06 (0.76,1.47)	0.728

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	**n**	**Number (%) Yes to Post-SEA Acne on Temples, Eyes, or, Ears**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Comparison	236	82 (34.7)		
Background RH	83	31 (37.3)	1.19 (0.70,2.02)	0.512
Low RH	57	21 (36.8)	1.12 (0.61,2.04)	0.723
High RH	61	21 (34.4)	0.94 (0.52,1.70)	0.833
Low plus High RH	118	42 (35.6)	1.02 (0.64,1.62)	0.935

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	236		
Background RH	83	1.20 (0.70,2.04)	0.503
Low RH	57	1.11 (0.61,2.04)	0.729
High RH	61	0.88 (0.48,1.63)	0.687
Low plus High RH	118	0.99 (0.62,1.58)	0.955

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes to Post-SEA Acne on Temples, Eyes, or, Ears	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	62	27 (43.5)	1.02 (0.86,1.21)	0.842
Medium	63	18 (28.6)		
High	76	28 (36.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
201	1.00 (0.83,1.21)	0.962

[a]Relative risk for a twofold increase in 1987 dioxin.

14.2.2.1.7 Duration of Post-SEA Acne (Excluding Participants with Pre-SEA Acne)

No significant group differences were revealed in the unadjusted and adjusted Model 1 analyses of duration of acne after service in SEA (excluding participants who reported acne prior to service in SEA) (Table 14-11(a,b): p>0.08 for each analysis).

Both the unadjusted and adjusted Model 2 analyses revealed significant positive associations between initial dioxin and duration of acne after service in SEA (Table 14-11(c,d): Slope=1.991, p<0.001; Adjusted Slope=1.808, p<0.001). The adjusted mean duration of acne after service in SEA in the low,

medium, and high initial dioxin categories was 17.75 months, 33.79 months, and 102.59 months, respectively.

The unadjusted Model 3 analysis revealed a significant difference in the duration of acne after service in SEA between Ranch Hands in the high dioxin category and Comparisons (Table 14-11(e): difference of means=63.97 months, p<0.001), as well as a significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 14-11(e): difference of means=27.75 months, p=0.032). After covariate adjustment, a significant difference was seen between Ranch Hands in the high dioxin category and Comparisons (Table 14-11(f): difference of adjusted means=54.28, p=0.002). Excluding participants who reported acne prior to service in SEA, the adjusted mean duration of acne after service in SEA was 104.25 months for Ranch Hands in the high dioxin category and 49.97 months for Comparisons. All remaining unadjusted and adjusted Model 3 contrasts were nonsignificant (Table 14-11(e,f): p>0.07 for each contrast).

The unadjusted and adjusted Model 4 analyses each revealed a significant positive association between 1987 dioxin and duration of acne after service in SEA (Table 14-11(g): Slope=1.103, p<0.001; Adjusted Slope=0.964, p=0.002). Excluding participants who reported acne prior to service in SEA, the adjusted mean duration of acne after service in SEA in the low, medium, and high 1987 dioxin categories was 29.90 months, 27.36 months, and 65.97 months, respectively.

Table 14-11. Analysis of Duration of Post-SEA Acne (Excluding Participants with Pre-SEA Acne) (months)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*88*	*67.88*	*15.23*	*0.172*
	Comparison	*86*	*52.66*		
Officer	Ranch Hand	18	48.11	15.45	0.406
	Comparison	23	32.66		
Enlisted Flyer	Ranch Hand	14	53.03	-40.25	0.197
	Comparison	12	93.28		
Enlisted Groundcrew	Ranch Hand	56	79.16	24.60	0.096
	Comparison	51	54.56		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*88*	*58.73*	*12.72*	*0.219*
	Comparison	*86*	*46.02*		
Officer	Ranch Hand	18	42.07	14.52	0.401
	Comparison	23	27.55		
Enlisted Flyer	Ranch Hand	14	45.63	-38.98	0.187
	Comparison	12	84.61		
Enlisted Groundcrew	Ranch Hand	56	72.49	23.99	0.089
	Comparison	51	48.49		

[a]Transformed from square root scale.

[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[c]P-value was based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for $\log_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	16	39.16	36.63	0.302	1.991 (0.423)	<0.001**
Medium	20	61.54	61.13			
High	20	151.91	156.65			

[a]Transformed from square root scale.

[b]Adjusted for body mass index at the time of the blood measurement of dioxin.

[c]Slope and standard error based on square root of duration of acne versus $\log_2$ (initial dioxin).

**: Statistically significant (p-value$\leq$0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 14-11. Analysis of Duration of Post-SEA Acne (Excluding Participants with Pre-SEA Acne) (months) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	16	17.75	0.349	1.808 (0.455)	<0.001**
Medium	20	33.79			
High	20	102.59			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of duration of acne versus $\log_2$ (initial dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	86	52.66	53.05		
Background RH	32	47.92	46.99	-6.06	0.656
Low RH	26	48.48	47.31	-5.74	0.697
High RH	30	115.56	117.02	63.97	<0.001**
Low plus High RH	56	80.85	80.80	27.75	0.032*

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	86	49.97		
Background RH	32	47.66	-2.31	0.867
Low RH	26	43.16	-6.81	0.637
High RH	30	104.25	54.28	0.002**
Low plus High RH	56	72.59	22.62	0.075

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

**: Statistically significant (p-value$\leq$0.010).

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	24	48.50	0.166	1.103 (0.267)	<0.001**
Medium	28	47.87			
High	36	102.33			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of duration of acne versus log_2 (1987 dioxin).

**: Statistically significant (p-value$\leq$0.010).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean**[a]	**R^2**	**Adjusted Slope (Standard Error)**[b]	**p-Value**
Low	24	29.90	0.206	0.964 (0.294)	0.002**
Medium	28	27.36			
High	36	65.97			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of duration of acne versus log$_2$ (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

14.2.2.1.8 Duration of Post-SEA Acne (All Post-SEA Occurrences)

All unadjusted and adjusted Model 1, 3, and 4 analyses of duration of acne after service in SEA were nonsignificant (Table 14-12(a,b,e-h): p>0.08 for each analysis).

The unadjusted Model 2 analysis showed a significant positive association between initial dioxin and duration of acne after service in SEA (when all participants with acne after service in SEA were included) (Table 14-12(c): Slope=0.903, p=0.034). After adjusting for covariates, however, the results were no longer significant (Table 14-12(d): p=0.067).

In comparing the results of this section and Section 14.2.2.1.7, it appears as if the significant relation between dioxin and the duration of acne after service in SEA appears to be confined to participants who did not report acne prior to service in SEA.

Table 14-12. Analysis of Duration of Post-SEA Acne (All Post-SEA Occurrences) (months)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*202*	*126.10*	*-8.49*	*0.549*
	Comparison	*231*	*134.59*		
Officer	Ranch Hand	53	121.23	-18.40	0.492
	Comparison	71	139.63		
Enlisted Flyer	Ranch Hand	33	113.86	-48.03	0.197
	Comparison	33	161.89		
Enlisted Groundcrew	Ranch Hand	116	131.99	6.78	0.718
	Comparison	127	125.21		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*202*	*107.71*	*-8.05*	*0.540*
	Comparison	*231*	*115.76*		
Officer	Ranch Hand	53	101.55	-16.09	0.511
	Comparison	71	117.63		
Enlisted Flyer	Ranch Hand	33	94.45	-44.65	0.191
	Comparison	33	139.09		
Enlisted Groundcrew	Ranch Hand	116	110.86	5.73	0.739
	Comparison	127	105.12		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	37	111.23	111.43	0.040	0.903 (0.420)	0.034*
Medium	42	101.30	101.32			
High	39	168.14	167.88			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of duration of acne versus log$_2$ (initial dioxin).

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	37	78.61	0.087	0.876 (0.474)	0.067
Medium	42	72.68			
High	39	126.42			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of duration of acne versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	231	134.59	134.52		
Background RH	83	126.10	126.57	-7.95	0.676
Low RH	57	98.99	99.05	-35.47	0.084
High RH	61	151.80	151.32	16.80	0.450
Low plus High RH	118	124.88	124.69	-9.83	0.554

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	231	117.84		
Background RH	83	109.81	-8.03	0.653
Low RH	57	86.91	-30.93	0.109
High RH	61	132.72	14.88	0.487
Low plus High RH	118	109.39	-8.45	0.590

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	63	138.18	0.006	0.298 (0.264)	0.259
Medium	63	104.18			
High	75	133.66			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of duration of acne versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	63	106.00	0.026	0.206 (0.288)	0.475
Medium	63	78.89			
High	75	95.47			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of duration of acne versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

14.2.2.2   Physical Examination Variables

14.2.2.2.1 Acneiform Lesions

No significant group differences were seen in the unadjusted and adjusted Model 1 analyses of acneiform lesions (Table 14-13(a,b): p>0.15 for each analysis).

A significant positive relation between initial dioxin and acneiform lesions was seen in the unadjusted Model 2 analysis (Table 14-13(c): Unadjusted RR=1.36, p=0.050). After adjusting for covariates, however, the results were nonsignificant (Table 14-13(d): p=0.467).

The unadjusted Model 3 analysis did not show any significant relation between dioxin category and acneiform lesions (Table 14-13(e): p>0.16 for each contrast). After covariate adjustment, a significant difference was seen between Ranch Hands in the background dioxin category and Comparisons (Table 14-13(f): Adjusted RR=1.72, p=0.042). The percentage of acneiform lesions was greater among Ranch Hands in the background dioxin category (6.5%) than Comparisons (4.9%).

The unadjusted and adjusted Model 4 analyses showed no significant associations between acneiform lesions and 1987 dioxin (Table 14-13(g,h): p>0.15 for each analysis).

Table 14-13. Analysis of Acneiform Lesions

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*45 (5.8)*	*1.18 (0.79,1.77)*	*0.413*
	Comparison	*1,174*	*58 (4.9)*		
Officer	Ranch Hand	307	12 (3.9)	1.40 (0.63,3.12)	0.404
	Comparison	462	13 (2.8)		
Enlisted Flyer	Ranch Hand	133	4 (3.0)	0.45 (0.14,1.42)	0.172
	Comparison	185	12 (6.5)		
Enlisted Groundcrew	Ranch Hand	337	29 (8.6)	1.41 (0.84,2.37)	0.195
	Comparison	527	33 (6.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,950*	*1.16 (0.77,1.73)*	*0.482*
Officer	769	1.44 (0.64,3.20)	0.376
Enlisted Flyer	318	0.43 (0.14,1.37)	0.155
Enlisted Groundcrew	863	1.34 (0.79,2.26)	0.274

(c) MODEL 2: RANCH HANDS − INITIAL DIOXIN − UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	1 (0.7)	1.36 (1.01,1.84)	0.050*
Medium	143	12 (8.4)		
High	141	9 (6.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS − INITIAL DIOXIN − ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
424	1.14 (0.80,1.63)	0.467

[a]Relative risk for a twofold increase in initial dioxin.

Table 14-13. Analysis of Acneiform Lesions (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	58 (4.9)		
Background RH	352	23 (6.5)	1.42 (0.86,2.35)	0.168
Low RH	211	6 (2.8)	0.55 (0.23,1.30)	0.173
High RH	213	16 (7.5)	1.49 (0.84,2.65)	0.177
Low plus High RH	424	22 (5.2)	0.91 (0.52,1.57)	0.730

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,173		
Background RH	352	1.72 (1.02,2.90)	0.042*
Low RH	211	0.58 (0.24,1.37)	0.214
High RH	213	1.08 (0.59,1.95)	0.805
Low plus High RH	424	0.79 (0.45,1.38)	0.406

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value$\leq$0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	19 (7.3)	0.99 (0.82,1.19)	0.920
Medium	258	5 (1.9)		
High	258	21 (8.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 14-13. Analysis of Acneiform Lesions (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
776	0.86 (0.71,1.06)	0.155

[a]Relative risk for a twofold increase in 1987 dioxin.

14.2.2.2.2 Acneiform Scars

All unadjusted and adjusted Model 1 through 4 analyses of acneiform scars were nonsignificant (Table 14-14(a-h): p>0.14 for each analysis).

Table 14-14. Analysis of Acneiform Scars

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*52 (6.7)*	*1.10 (0.76,1.59)*	*0.621*
	Comparison	*1,174*	*72 (6.1)*		
Officer	Ranch Hand	307	18 (5.9)	1.45 (0.75,2.81)	0.269
	Comparison	462	19 (4.1)		
Enlisted Flyer	Ranch Hand	133	14 (10.5)	1.70 (0.76,3.80)	0.199
	Comparison	185	12 (6.5)		
Enlisted Groundcrew	Ranch Hand	337	20 (5.9)	0.75 (0.43,1.30)	0.303
	Comparison	527	41 (7.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,950*	*1.04 (0.72,1.52)*	*0.824*
Officer	769	1.51 (0.77,2.95)	0.230
Enlisted Flyer	318	1.63 (0.71,3.71)	0.246
Enlisted Groundcrew	863	0.67 (0.38,1.18)	0.166

Table 14-14. Analysis of Acneiform Scars (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Yes**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	140	6 (4.3)	1.08 (0.79,1.46)	0.640
Medium	143	11 (7.7)		
High	141	7 (5.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
424	1.03 (0.71,1.49)	0.877

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	72 (6.1)		
Background RH	352	27 (7.7)	1.32 (0.83,2.10)	0.241
Low RH	211	11 (5.2)	0.83 (0.43,1.60)	0.580
High RH	213	13 (6.1)	0.96 (0.52,1.78)	0.904
Low plus High RH	424	24 (5.7)	0.90 (0.55,1.44)	0.650

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 14-14. Analysis of Acneiform Scars (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,173		
Background RH	352	1.43 (0.88,2.32)	0.148
Low RH	211	0.81 (0.41,1.57)	0.526
High RH	213	0.77 (0.41,1.46)	0.422
Low plus High RH	424	0.79 (0.48,1.29)	0.339

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	22 (8.5)	0.88 (0.73,1.05)	0.151
Medium	258	12 (4.7)		
High	258	17 (6.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
776	0.87 (0.71,1.06)	0.166

[a]Relative risk for a twofold increase in 1987 dioxin.

14.2.2.2.3 Comedones

No significant group differences were revealed in the unadjusted Model 1 analysis of comedones (Table 14-15(a): p>0.05 for each analysis). Adjusting for covariates showed no group differences over all participants (Table 14-15(b): p=0.131). After stratifying the adjusted analysis by military occupation, a significant difference between Ranch Hand and Comparison officers was seen (Table 14-15(b): Adjusted RR=0.46, p=0.049). Fewer Ranch Hand officers had comedones than Comparison officers (2.9% versus 6.1%, respectively). Other Model 1 adjusted contrasts were nonsignificant (Table 14-15(b): p>0.26 for all remaining contrasts).

All unadjusted and adjusted Model 2, 3, and 4 analyses were nonsignificant (Table 14-15(c-h): p>0.05 for each analysis).

Table 14-15. Analysis of Comedones

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*41 (5.3)*	*0.77 (0.52,1.14)*	*0.187*
	Comparison	*1,174*	*79 (6.7)*		
Officer	Ranch Hand	307	9 (2.9)	0.47 (0.22,1.01)	0.052
	Comparison	462	28 (6.1)		
Enlisted Flyer	Ranch Hand	133	11 (8.3)	0.70 (0.33,1.52)	0.370
	Comparison	185	21 (11.4)		
Enlisted Groundcrew	Ranch Hand	337	21 (6.2)	1.10 (0.62,1.96)	0.743
	Comparison	527	30 (5.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,950*	*0.74 (0.50,1.10)*	*0.131*
Officer	769	0.46 (0.21,1.00)	0.049*
Enlisted Flyer	318	0.65 (0.30,1.40)	0.269
Enlisted Groundcrew	863	1.10 (0.61,1.96)	0.755

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	4 (2.9)	1.31 (0.96,1.79)	0.094
Medium	143	9 (6.3)		
High	141	8 (5.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 14-15. Analysis of Comedones (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
424	1.44 (1.00,2.09)	0.052

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Black Ranch Hands with comedones.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	79 (6.7)		
Background RH	352	19 (5.4)	0.78 (0.46,1.31)	0.345
Low RH	211	8 (3.8)	0.55 (0.26,1.15)	0.113
High RH	213	13 (6.1)	0.91 (0.50,1.68)	0.769
Low plus High RH	424	21 (5.0)	0.71 (0.43,1.18)	0.182

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,173		
Background RH	352	0.82 (0.48,1.39)	0.458
Low RH	211	0.47 (0.22,1.01)	0.052
High RH	213	0.85 (0.45,1.59)	0.603
Low plus High RH	424	0.63 (0.38,1.06)	0.084

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 14-15. Analysis of Comedones (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	15 (5.8)	0.98 (0.81,1.20)	0.864
Medium	258	10 (3.9)		
High	258	15 (5.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
776	0.87 (0.71,1.08)	0.222

[a]Relative risk for a twofold increase in 1987 dioxin.

14.2.2.2.4 Depigmentation

No significant associations with dioxin were revealed in the unadjusted and adjusted Model 1 through 4 analyses of depigmentation (Table 14-16(a-h): p≥0.08 for each analysis).

Table 14-16. Analysis of Depigmentation

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*17 (2.2)*	*0.71 (0.39,1.27)*	*0.236*
	Comparison	*1,174*	*36 (3.1)*		
Officer	Ranch Hand	307	6 (2.0)	0.90 (0.32,2.51)	0.842
	Comparison	462	10 (2.2)		
Enlisted Flyer	Ranch Hand	133	5 (3.8)	1.17 (0.35,3.90)	0.804
	Comparison	185	6 (3.2)		
Enlisted Groundcrew	Ranch Hand	337	6 (1.8)	0.46 (0.18,1.16)	0.099
	Comparison	527	20 (3.8)		

Table 14-16. Analysis of Depigmentation (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,950*	*0.71 (0.39,1.27)*	*0.236*
Officer	769	0.89 (0.32,2.47)	0.823
Enlisted Flyer	318	1.16 (0.35,3.90)	0.810
Enlisted Groundcrew	863	0.47 (0.18,1.17)	0.105

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	5 (3.6)	1.06 (0.69,1.62)	0.800
Medium	143	2 (1.4)		
High	141	5 (3.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
424	1.21 (0.71,2.04)	0.492

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	36 (3.1)		
Background RH	352	4 (1.1)	0.39 (0.14,1.12)	0.080
Low RH	211	7 (3.3)	1.05 (0.46,2.40)	0.906
High RH	213	5 (2.3)	0.70 (0.27,1.83)	0.471
Low plus High RH	424	12 (2.8)	0.86 (0.44,1.69)	0.661

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 14-16. Analysis of Depigmentation (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,173		
Background RH	352	0.42 (0.15,1.21)	0.110
Low RH	211	1.03 (0.45,2.36)	0.947
High RH	213	0.68 (0.26,1.80)	0.434
Low plus High RH	424	0.83 (0.42,1.65)	0.601

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	3 (1.2)	1.23 (0.91,1.65)	0.182
Medium	258	7 (2.7)		
High	258	6 (2.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
776	1.35 (0.92,1.97)	0.116

[a]Relative risk for a twofold increase in 1987 dioxin.

14.2.2.2.5 Hyperpigmentation

All unadjusted and adjusted Model 1 through 4 analyses of hyperpigmentation were nonsignificant (Table 14-17(a-h): p>0.10 for each analysis).

Table 14-17. Analysis of Hyperpigmentation

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*53 (6.8)*	*0.84 (0.59,1.19)*	*0.329*
	Comparison	*1,174*	*94 (8.0)*		
Officer	Ranch Hand	307	17 (5.5)	0.76 (0.42,1.39)	0.378
	Comparison	462	33 (7.1)		
Enlisted Flyer	Ranch Hand	133	10 (7.5)	0.80 (0.36,1.82)	0.599
	Comparison	185	17 (9.2)		
Enlisted Groundcrew	Ranch Hand	337	26 (7.7)	0.92 (0.55,1.52)	0.739
	Comparison	527	44 (8.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,950*	*0.84 (0.59,1.20)*	*0.334*
Officer	769	0.74 (0.41,1.36)	0.340
Enlisted Flyer	318	0.79 (0.35,1.79)	0.566
Enlisted Groundcrew	863	0.95 (0.57,1.57)	0.828

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	14 (10.0)	0.80 (0.61,1.06)	0.114
Medium	143	14 (9.8)		
High	141	7 (5.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
424	0.77 (0.56,1.07)	0.108

[a]Relative risk for a twofold increase in initial dioxin.

Table 14-17. Analysis of Hyperpigmentation (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	94 (8.0)		
Background RH	352	18 (5.1)	0.72 (0.43,1.22)	0.221
Low RH	211	18 (8.5)	1.00 (0.59,1.72)	0.992
High RH	213	17 (8.0)	0.86 (0.50,1.49)	0.593
Low plus High RH	424	35 (8.3)	0.93 (0.61,1.41)	0.727

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,173		
Background RH	352	0.75 (0.44,1.28)	0.295
Low RH	211	0.95 (0.55,1.63)	0.838
High RH	213	0.91 (0.52,1.61)	0.747
Low plus High RH	424	0.93 (0.61,1.41)	0.726

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	11 (4.2)	0.99 (0.83,1.18)	0.925
Medium	258	24 (9.3)		
High	258	18 (7.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 14-17. Analysis of Hyperpigmentation (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
776	0.96 (0.79,1.17)	0.696

[a]Relative risk for a twofold increase in 1987 dioxin.

14.2.2.2.6 Inclusion Cysts

No significant associations with dioxin were revealed in the unadjusted and adjusted Model 1 through 4 analyses of inclusion cysts (Table 14-18(a-h): p>0.13 for each analysis).

Table 14-18. Analysis of Inclusion Cysts

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*98 (12.6)*	*1.12 (0.85,1.48)*	*0.425*
	Comparison	*1,174*	*134 (11.4)*		
Officer	Ranch Hand	307	27 (8.8)	0.71 (0.44,1.16)	0.173
	Comparison	462	55 (11.9)		
Enlisted Flyer	Ranch Hand	133	23 (17.3)	1.55 (0.82,2.92)	0.175
	Comparison	185	22 (11.9)		
Enlisted Groundcrew	Ranch Hand	337	48 (14.2)	1.37 (0.91,2.07)	0.134
	Comparison	527	57 (10.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,950*	*1.10 (0.83,1.46)*	*0.490*
Officer	769	0.71 (0.44,1.16)	0.171
Enlisted Flyer	318	1.50 (0.80,2.83)	0.210
Enlisted Groundcrew	863	1.35 (0.90,2.05)	0.151

Table 14-18. Analysis of Inclusion Cysts (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	12 (8.6)	1.10 (0.89,1.36)	0.373
Medium	143	23 (16.1)		
High	141	19 (13.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
424	1.09 (0.85,1.40)	0.485

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	134 (11.4)		
Background RH	352	43 (12.2)	1.10 (0.76,1.59)	0.614
Low RH	211	23 (10.9)	0.94 (0.59,1.51)	0.811
High RH	213	31 (14.6)	1.30 (0.85,1.99)	0.222
Low plus High RH	424	54 (12.7)	1.11 (0.79,1.56)	0.550

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 14-18.   Analysis of Inclusion Cysts (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,173		
Background RH	352	1.13 (0.78,1.65)	0.519
Low RH	211	0.91 (0.57,1.46)	0.704
High RH	213	1.22 (0.79,1.89)	0.371
Low plus High RH	424	1.06 (0.75,1.49)	0.756

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	28 (10.8)	1.10 (0.96,1.25)	0.159
Medium	258	30 (11.6)		
High	258	39 (15.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
776	1.03 (0.89,1.20)	0.660

[a]Relative risk for a twofold increase in 1987 dioxin.

14.2.2.2.7 Dermatology Index

The dermatology index was constructed from the results of the physical examination of comedones, acneiform lesions, acneiform scars, and inclusion cysts. All unadjusted and adjusted Model 1, 3, and 4 analyses showed no significant associations with dermatology index (Table 14-19(a,b,e-h): p>0.08 for each analysis).

A significant positive relation with initial dioxin was seen in the unadjusted Model 2 analysis of dermatology index (Table 14-19(c): Unadjusted RR=1.20, p=0.034). After adjusting for covariates, however, the results were no longer significant (Table 14-19(d): p=0.115).

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Table 14-19. Analysis of Dermatology Index

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*184 (23.7)*	*1.00 (0.81,1.24)*	*0.965*
	Comparison	*1,174*	*277 (23.6)*		
Officer	Ranch Hand	307	54 (17.6)	0.84 (0.58,1.21)	0.343
	Comparison	462	94 (20.3)		
Enlisted Flyer	Ranch Hand	133	40 (30.1)	1.19 (0.73,1.96)	0.482
	Comparison	185	49 (26.5)		
Enlisted Groundcrew	Ranch Hand	337	90 (26.7)	1.07 (0.78,1.46)	0.676
	Comparison	527	134 (25.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,950*	*0.98 (0.79,1.22)*	*0.855*
Officer	769	0.84 (0.57,1.21)	0.347
Enlisted Flyer	318	1.14 (0.69,1.88)	0.609
Enlisted Groundcrew	863	1.04 (0.76,1.42)	0.828

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	20 (14.3)	1.20 (1.01,1.41)	0.034*
Medium	143	42 (29.4)		
High	141	37 (26.2)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for $\log_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
424	1.17 (0.96,1.42)	0.115

[a]Relative risk for a twofold increase in initial dioxin.

Table 14-19. Analysis of Dermatology Index (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	277 (23.6)		
Background RH	352	84 (23.9)	1.05 (0.79,1.39)	0.742
Low RH	211	40 (19.0)	0.75 (0.52,1.09)	0.127
High RH	213	59 (27.7)	1.21 (0.87,1.68)	0.266
Low plus High RH	424	99 (23.3)	0.95 (0.73,1.24)	0.717

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,173		
Background RH	352	1.14 (0.85,1.52)	0.387
Low RH	211	0.72 (0.49,1.04)	0.083
High RH	213	1.02 (0.73,1.45)	0.890
Low plus High RH	424	0.86 (0.65,1.13)	0.268

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	63 (24.2)	1.05 (0.94,1.16)	0.396
Medium	258	47 (18.2)		
High	258	73 (28.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 14-19. Analysis of Dermatology Index (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log_2 (1987 Dioxin) | |
| | Adjusted Relative Risk | |
n	(95% C.I.)[a]	p-Value
776	0.97 (0.86,1.09)	0.578

[a]Relative risk for a twofold increase in 1987 dioxin.

14.3 DISCUSSION

Chloracne has very salient diagnostic features in both its distribution and physical findings that differentiates it from other forms of acne and "acne variants." Chemical workers manufacturing chlorophenol or organochlorine pesticides are most likely to develop chloracne. One of the goals of the AFHS was to evaluate the occurrence of chloracne in participants exposed to herbicides and dioxin. Signs of chloracne were assessed through self-reporting (interviews) and physical examination.

Chloracne distribution usually involves the periorbital and malar areas, temples, posterior auricular sites, extensor aspects of the arms and legs, and, on occasion, the periumbilical and genital regions. According to medical records reviews, no cases of acne on the periumbilical and genital regions were reported for the 2002 physical examination. Lesions that would be key physical findings of chloracne may include closed and open comedones, fluid-filled cysts, and uninflamed papules and nodules. Other cutaneous findings, such as scarring, hyperpigmentation, and depigmentation, are secondary findings and are only indirectly related to chloracne.

As expected, no cases of chloracne were identified at the 2002 physical examination. In fact, no cases of chloracne have been identified over the 20-year examination period of the AFHS. The historical presence of acne, as determined through participant-reported occurrences of acne, was investigated to examine if associations related to herbicide or dioxin exposure may have existed that would be suggestive of chloracne in the past. Because self-reporting of acne is extremely subjective, conditions such as rosacea (in which papules and pustules share clinical features with those observed in acne vulgaris [common acne]); seborrheic dermatitis (a chronic skin disease associated with seborrhea and greasy scales on the scalp or eyelids or other parts of the skin); pseudofolliculitis barbae (an extrafollicular or transfollicular ingrown hair penetration accompanied by inflammation in 45 to 83 percent of Blacks who shave regularly); and Favre-Racouchot syndrome (nodular elastosis with facial cysts and comedones due to aging, sun exposure, or smoking, as seen in 6 percent of people, most commonly Caucasian males aged 40 to 60) may be self-reported as acne (103-106). Tropical acne (inflammatory lesions occurring primarily on the trunk or possibly on the face) (107) is caused by a hot, humid environment and should not be considered a problem that would be newly observed at the 2002 physical examination due to the participants' advancing ages and their current residences being in less tropical environments than SEA.

Acne vulgaris is a condition that primarily affects younger individuals. It is most severe in the 16- to 24-year-old age group. The reporting of acne after service in SEA and the increased acneiform lesions and acneiform scarring is to be expected in the younger participants. Comedones (Favre-Racouchot syndrome) and hyperpigmentation (poikiloderma of Civatte, hemosiderin deposition in the skin secondary to ecchymoses) are commonly seen in older patients and not necessarily related to acne.

Hyperpigmentation usually occurs in individuals with Type V or VI (Black) skin types and after acne and other inflammatory cutaneous disorders. Black participants reported acne more often than non-Black participants after service in SEA, but the acne was of shorter duration, on average, and with fewer comedones, lesions, scars, and inclusion cysts. These results may be explained if Black participants reported pseudofolliculitis barbae as acne.

If a participant already had acne prior to duty in SEA, it is expected that the dermatology index will be more severe in this group than for participants who did not have acne prior to service in SEA. In addition, environmental factors aggravate already existing acne.

The evaluation of chloracne was based on physical examination only. Occupational history after service in SEA was not used to identify participants who potentially may have been at risk for developing chloracne. No biopsies to confirm the diagnosis of chloracne were deemed necessary by the examining physicians. Chloracne usually appears after a short interval of exposure to dioxin, without a long latency period, and usually persists for 2 to 3 years. Therefore, primary lesions were not expected to be noted upon physical examination. No differences were found between the Ranch Hand and Comparison groups in terms of secondary lesions (scarring, hyperpigmentation, and depigmentation). If secondary lesions had been observed, chloracne might be suggested if the lesions had been found in the typical distribution areas of chloracne. In essence, based on the results of the 2002 physical examination, there were no primary or secondary dermatological findings between the Ranch Hand and Comparison groups that would suggest chloracne.

For Ranch Hands who had a 1987 dioxin measurement of greater than 10 ppt, lipid adjusted serum dioxin levels were extrapolated to an estimated initial dioxin at the end of the last qualifying tour of duty. The median of Ranch Hands with an estimated initial dioxin was 118 ppt, which was less than the serum dioxin levels for which chloracne has been reported (300-400 ppt) in the literature (60).

Self-reported information on acne included the lifetime occurrence, the occurrence in relation to time of duty, and the location. Because the majority of participants who reported acne did not visit a physician for the acne, verification from a medical records review was not feasible. Acneiform lesions, acneiform scars, comedones, and inclusion cysts were used to comprise a dermatology index. Hyperpigmentation and depigmentation were investigated as well. If any of these conditions was present, the result was tabulated as abnormal.

Acne was increased in Ranch Hand enlisted groundcrew, the subgroup with the highest median dioxin level. An increase in acne was also found in the 1992 follow-up examination report. This increase requires more study to determine the relation, if any, between acne and other factors not considered in this report, including the dates of service, the number of days served in the Ranch Hand unit, and occupational exposure history to herbicides and other chemicals. Differences between Ranch Hand enlisted flyers and enlisted groundcrew with regard to these factors may be informative.

Acne was increased in Ranch Hand enlisted groundcrew, in parallel with an increase found at the 1992 physical examination. This occupational category was not separately assessed for the reports of the 1982, 1985, or 1987 examinations, and dermatological conditions were not analyzed for the 1997 follow-up examination report. Further study is required to assess the relation, if any, between this increase and other factors not considered in this report.

The reason for the higher occurrence of acne in Ranch Hand enlisted groundcrew is unknown. Significant findings were present, but they were seen in self-reported data on acne and not substantiated

by findings on the physical examination. In addition, Ranch Hands in the background dioxin category had a higher percentage of acneiform lesions, but not in the low or high dioxin categories.

In conclusion, there does not appear to be a dose-response relation between herbicide exposure or dioxin and acne, based on physical examination findings. In addition, the relatively low amount of serum dioxin makes the increases in the self-reported acne in all Ranch Hand dioxin categories relative to Comparisons difficult to interpret.

14.4 SUMMARY

The dermatology assessment was based on physical examination data and self-reported questionnaire data regarding occurrence, location, and duration of acne. Associations with herbicide exposure (i.e., group − Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable in the dermatology assessment. The significant adjusted results are discussed in the sections below.

14.4.1 Model 1: Group Analysis

Ranch Hands reported acne over their lifetime and acne after service in SEA more often than Comparisons did. This result was also seen for enlisted groundcrew. These significant results were restricted to participants who did not have acne prior to service in SEA. In addition, Ranch Hand officers had fewer comedones than Comparison officers. The results of the group analysis are shown in Table 14-20.

Table 14-20. Summary of Group Analysis (Model 1) for Dermatology Variables (Ranch Hands vs. Comparisons)

| Variable | UNADJUSTED | | | |
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Questionnaire				
Acne (lifetime) (D)	p=0.003 (1.32)	ns	NS	p<0.001 (1.64)
Post-SEA Acne (D)	p=0.002 (1.40)	NS	NS	p=0.001 (1.62)
Post-SEA Acne (no pre-SEA acne) (D)	p=0.001 (1.70)	NS	NS	p<0.001 (2.14)
Post-SEA Acne (with pre-SEA acne) (D)	NS	NS	NS	NS
Location of Post-SEA Acne (excluding participants with pre-SEA acne) (D)	NS	ns	ns	NS
Location of Post-SEA Acne (all post-SEA occurrences) (D)	NS	NS	ns	NS
Duration of Post-SEA Acne (excluding participants with pre-SEA acne) (C)	NS	NS	ns	NS
Duration of Post-SEA Acne (all post-SEA occurrences) (C)	ns	ns	ns	NS
Physical Examination				
Acneiform Lesions (D)	NS	NS	ns	NS
Acneiform Scars (D)	NS	NS	NS	ns
Comedones (D)	ns	ns	ns	NS
Depigmentation (D)	ns	ns	NS	ns
Hyperpigmentation (D)	ns	ns	ns	ns

	UNADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Inclusion Cysts (D)	NS	ns	NS	NS
Dermatology Index (D)	NS	ns	NS	NS

Note: NS or ns: Not significant (p>0.05).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

	ADJUSTED			
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Questionnaire				
Acne (lifetime) (D)	p=0.002 (1.34)	NS	NS	p<0.001 (1.61)
Post-SEA Acne (D)	p=0.001 (1.43)	NS	NS	p=0.003 (1.60)
Post-SEA Acne (no pre-SEA acne) (D)	p<0.001 (1.78)	NS	NS	p<0.001 (2.15)
Post-SEA Acne (with pre-SEA acne) (D)	NS	NS	NS	NS
Location of Post-SEA Acne (excluding participants with pre-SEA acne) (D)	ns	ns	ns	NS
Location of Post-SEA Acne (all post-SEA occurrences) (D)	NS	NS	ns	NS
Duration of Post-SEA Acne (excluding participants with pre-SEA acne) (C)	NS	NS	ns	NS
Duration of Post-SEA Acne (all post-SEA occurrences) (C)	ns	ns	ns	NS
Physical Examination				
Acneiform Lesions (D)	NS	NS	ns	NS
Acneiform Scars (D)	NS	NS	NS	ns
Comedones (D)	ns	p=0.049 (0.46)	ns	NS
Depigmentation (D)	ns	ns	NS	ns
Hyperpigmentation (D)	ns	ns	ns	ns
Inclusion Cysts (D)	NS	ns	NS	NS
Dermatology Index (D)	ns	ns	NS	NS

Note: NS or ns: Not significant (p>0.05).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

14.4.2 Model 2: Initial Dioxin Analysis

A significant positive association was seen between initial dioxin and duration of reported acne after service in SEA, when participants with acne prior to service in SEA were excluded. The results of all unadjusted and adjusted Model 2 analyses are summarized in Table 14-21.

Table 14-21. Summary of Initial Dioxin Analysis (Model 2) for Dermatology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Questionnaire		
Acne (lifetime) (D)	ns	ns
Post-SEA Acne (D)	NS	ns
Post-SEA Acne (no pre-SEA acne) (D)	NS	ns
Post-SEA Acne (with pre-SEA acne) (D)	NS	NS
Location of Post-SEA Acne (excluding participants with pre-SEA acne) (D)	NS	NS
Location of Post-SEA Acne (all post-SEA occurrences) (D)	NS	NS
Duration of Post-SEA Acne (excluding participants with pre-SEA acne) (C)	p<0.001 (1.991)	p<0.001 (1.808)
Duration of Post-SEA Acne (all post-SEA occurrences) (C)	p=0.034 (0.903)	NS
Physical Examination		
Acneiform Lesions (D)	p=0.050 (1.36)	NS
Acneiform Scars (D)	NS	NS
Comedones (D)	NS	NS
Depigmentation (D)	NS	NS
Hyperpigmentation (D)	ns	ns
Inclusion Cysts (D)	NS	NS
Dermatology Index (D)	p=0.034 (1.20)	NS

Note: NS or ns: Not significant (p>0.05).
    C: Continuous form of dependent variable.
    D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

14.4.3 Model 3: Categorized Dioxin Analysis

Ranch Hands in the background dioxin category, in the low dioxin category, and in the low and high dioxin categories combined reported acne more often than Comparisons did. Upon further investigation, the acne was observed to be after service in SEA and, in particular, for participants who did not have acne prior to service in SEA. Ranch Hands in the high dioxin category without acne prior to service in SEA also reported a longer duration of acne after service in SEA than Comparisons without acne prior to service in SEA. In addition, Ranch Hands in the background dioxin category had more acneiform lesions than Comparisons. The results of all unadjusted and adjusted Model 3 analyses are summarized in Table 14-22.

Table 14-22. Summary of Categorized Dioxin Analysis (Model 3) for Dermatology Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Questionnaire				
Acne (lifetime) (D)	NS	p=0.010 (1.48)	p=0.019 (1.42)	p=0.001 (1.45)
Post-SEA Acne (D)	NS	p=0.023 (1.47)	p=0.006 (1.58)	p=0.001 (1.53)
Post-SEA Acne (no pre-SEA acne) (D)	NS	p=0.005 (1.99)	p<0.001 (2.19)	p<0.001 (2.09)
Post-SEA Acne (with pre-SEA acne) (D)	NS	NS	NS	NS
Location of Post-SEA Acne (excluding participants with pre-SEA acne) (D)	ns	ns	NS	NS
Location of Post-SEA Acne (all post-SEA occurrences) (D)	NS	NS	ns	NS
Duration of Post-SEA Acne (excluding participants with pre-SEA acne) (C)	ns	ns	p<0.001 (63.97)	p=0.032 (27.75)
Duration of Post-SEA Acne (all post-SEA occurrences) (C)	ns	ns	NS	ns
Physical Examination				
Acneiform Lesions (D)	NS	ns	NS	ns
Acneiform Scars (D)	NS	ns	ns	ns
Comedones (D)	ns	ns	ns	ns
Depigmentation (D)	ns	NS	ns	ns
Hyperpigmentation (D)	ns	NS	ns	ns
Inclusion Cysts (D)	NS	ns	NS	NS
Dermatology Index (D)	NS	ns	NS	ns

Note: NS or ns: Not significant (p>0.05).
     C: Continuous form of dependent variable.
     D: Discrete form of dependent variable.

     The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

     A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

	ADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Questionnaire				
Acne (lifetime) (D)	NS	p=0.002 (1.63)	NS	p=0.002 (1.45)
Post-SEA Acne (D)	p=0.009 (1.49)	p=0.003 (1.68)	NS	p=0.011 (1.41)
Post-SEA Acne (no pre-SEA acne) (D)	p=0.046 (1.60)	p=0.002 (2.19)	p=0.026 (1.72)	p<0.001 (1.93)
Post-SEA Acne (with pre-SEA acne) (D)	NS	NS	ns	ns
Location of Post-SEA Acne (excluding participants with pre-SEA acne) (D)	NS	ns	ns	ns
Location of Post-SEA Acne (all post-SEA occurrences) (D)	NS	NS	ns	ns
Duration of Post-SEA Acne (excluding participants with pre-SEA acne) (C)	ns	ns	p=0.002 (54.28)	NS
Duration of Post-SEA Acne (all post-SEA occurrences) (C)	ns	ns	NS	ns
Physical Examination				
Acneiform Lesions (D)	p=0.042 (1.72)	ns	NS	ns
Acneiform Scars (D)	NS	ns	ns	ns
Comedones (D)	ns	ns	ns	ns
Depigmentation (D)	ns	NS	ns	ns
Hyperpigmentation (D)	ns	ns	ns	ns
Inclusion Cysts (D)	NS	ns	NS	NS
Dermatology Index (D)	NS	ns	NS	ns

Note: NS or ns: Not significant (p>0.05).

      C: Continuous form of dependent variable.

      D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

14.4.4 Model 4: 1987 Dioxin Level Analysis

For participants who did not have acne prior to service in SEA, the mean duration of acne after service in SEA increased with 1987 dioxin. All results for Model 4 unadjusted and adjusted analyses are summarized in Table 14-23.

Table 14-23. Summary of 1987 Dioxin Analysis (Model 4) for Dermatology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Questionnaire		
Acne (lifetime) (D)	NS	ns
Post-SEA Acne (D)	NS	ns
Post-SEA Acne (no pre-SEA acne) (D)	NS	ns
Post-SEA Acne (with pre-SEA acne) (D)	NS	ns
Location of Post-SEA Acne (excluding participants with pre-SEA acne) (D)	NS	NS
Location of Post-SEA Acne (all post-SEA occurrences) (D)	NS	NS
Duration of Post-SEA Acne (excluding participants with pre-SEA acne) (C)	p<0.001 (1.103)	p=0.002 (0.964)
Duration of Post-SEA Acne (all post-SEA occurrences) (C)	NS	NS
Physical Examination		
Acneiform Lesions (D)	ns	ns
Acneiform Scars (D)	ns	ns
Comedones (D)	ns	ns
Depigmentation (D)	NS	NS
Hyperpigmentation (D)	ns	ns
Inclusion Cysts (D)	NS	NS
Dermatology Index (D)	NS	ns

Note: NS or ns: Not significant (p>0.05).

  C: Continuous form of dependent variable.

  D: Discrete form of dependent variable.

  The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

  A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

14.4.5 Summary of Significant Results

Table 14-24 summarizes the significant results (p≤0.05) for the adjusted analyses that were performed for the dermatology assessment. The dependent variable and its table reference are listed along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and is explained in footnotes.

Table 14-24. Summary of Results from Significant Adjusted Analyses in the Dermatology Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Occurrence of Acne (Lifetime) (14-3)	1	RH vs. C, All	0.002	1.34 (1.11,1.61)	RH: 47.5% C: 40.6%	(a)
	1	RH vs. C, Enlisted Groundcrew	<0.001	1.61 (1.22,2.14)	RH: 52.8% C: 40.6%	(a)
	3	Low RH vs. C	0.002	1.63 (1.20,2.20)	RH: 50.2% C: 40.6%	(b)
	3	Low plus High RH vs. C	0.002	1.45 (1.15,1.83)	RH: 49.8% C: 40.6%	(b)
Post-SEA Acne (14-4)	1	RH vs. C, All	0.001	1.43 (1.15,1.78)	RH: 26.4% C: 20.4%	(a)
	1	RH vs. C, Enlisted Groundcrew	0.003	1.60 (1.18,2.16)	RH: 35.0% C: 24.9%	(a)
	3	Background RH vs. C	0.009	1.49 (1.10,2.01)	RH: 23.9% C: 20.4%	(b)
	3	Low RH vs. C	0.003	1.68 (1.19,2.37)	RH: 27.5% C: 20.4%	(b)
	3	Low plus High RH vs. C	0.011	1.41 (1.08,1.83)	RH: 28.3% C: 20.4%	(b)
Post-SEA Acne (no pre-SEA acne) (14-5)	1	RH vs. C, All	<0.001	1.78 (1.29,2.46)	RH: 18.0% C: 11.4%	(a)
	1	RH vs. C, Enlisted Groundcrew	<0.001	2.15 (1.40,3.29)	RH: 26.3% C: 14.2%	(a)
	3	Background RH vs. C	0.046	1.60 (1.01,2.53)	RH: 14.1% C: 11.4%	(b)
	3	Low RH vs. C	0.002	2.19 (1.34,3.58)	RH: 20.5% C: 11.4%	(b)
	3	High RH vs. C	0.026	1.72 (1.07,2.78)	RH: 22.1% C: 11.4%	(b)
	3	Low plus High RH vs. C	<0.001	1.93 (1.33,2.82)	RH: 21.3% C: 11.4%	(b)
Duration of Post-SEA Acne (no pre-SEA acne) (14-11)	2	RH (1987 Dioxin >10 ppt): Initial Dioxin	<0.001	1.808 (0.455)	Low: 17.75 months Medium: 33.79 months High: 102.59 months	(c)
	3	High RH vs. C	0.002	54.28	RH: 104.25 months C: 49.97 months	(d)
	4	All RH: 1987 Dioxin	0.002	0.964 (0.294)	Low: 29.90 months Medium: 27.36 months High: 65.97 months	(e)
Acneiform Lesions (14-13)	3	Background RH vs. C	0.042	1.72 (1.02,2.90)	RH: 6.5% C: 4.9%	(b)
Comedones (14-15)	1	RH vs. C, Officer	0.049	0.46 (0.21,1.00)	RH: 2.9% C: 6.1%	(a)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(c): Continuous variable: slope and standard error were presented and were based on square root of dependent variable versus $\log_2$ (initial dioxin); adjusted means were transformed to original scale and were presented for each of three initial dioxin categories.

(d): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were transformed to original scale and were presented for each dioxin category in contrast.

(e): Continuous variable: slope and standard error were presented and were based on square root of dependent variable versus $\log_2$ (1987 dioxin); adjusted means were transformed to original scale and were presented for each of three 1987 dioxin categories.

Note: RH = Ranch Hand.
        C = Comparison.

   Model 2:   Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt).

   Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
              Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
              High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

   Model 4:   Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

14.5 CONCLUSION

Chloracne is a skin condition recognized as a consequence of exposure to high levels of dioxin and other cyclic organochlorine compounds. It usually appears without long latency after a short interval of exposure to dioxin and persists for about 2 to 3 years. Primary lesions of chloracne were not expected to persist and be noted upon physical examination in 2002. Chloracne might be suggested if the secondary lesions such as scarring, hyperpigmentation, and depigmentation had been observed in the typical distribution areas of chloracne around eyes, temples, and ears. No evidence of chloracne was found in the Ranch Hand or Comparison group.

The dermatology assessment included the occurrence of self-reported acne and physical examination. The occurrence and duration of acne were reported by the participants at the 2002 physical examination. The frequency and occurrence of reported acne after service in SEA were increased in Ranch Hand enlisted groundcrew, the subgroup with the highest median dioxin levels. The frequency of reported acne since SEA service was increased in the background, low, and high dioxin exposure categories. The frequency of acneiform lesions on physical examination was increased only in the background category. The duration of reported acne after service in SEA increased with 1987 dioxin.

The interpretation of the increased frequency of reported acne after service in SEA in Ranch Hand enlisted groundcrew is uncertain because secondary lesions that were observed revealed no association with herbicide or dioxin exposure.

REFERENCES

1. Kammig, J., and K.H. Schulz. 1957. Occupational acne due to chlorinated aromatic cyclic esters. *Dermatologica* 115:540.

2. Kammig, J., and K.H. Schulz. 1957. Chlorinated aromatic cyclic ethers as the cause of so-called chloracne. *Naturwissenschaften* 44:337-8.

3. Kimbrough, R.D. 1980. Occupational exposure. In: Halogenated Biphenyls, Terphenyls, Naphthalenes, Dibenzodioxins, and Related Products. R.D. Kimbrough, ed. Elsevier: Amsterdam, North Holland.

4. Suskind, R.R., and V.S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *The Journal of the American Medical Association* 251:2372-80.

5. Crow, K.D. 1981. Chloracne and its potential clinical implications. *Clinical and Experimental Dermatology* 6:243-57.

6. Crow, K.D. 1983. Significance of cutaneous lesions in the symptomatology of exposure to dioxins and other chloracnegens. In: Human and Environmental Risks of Chlorinated Dioxins and Related Compounds. R.E. Tucker, A.L. Young, and A.P. Gray, eds. Plenum Press: New York, NY.

7. Bleiberg, J., M. Wallen, R. Brodkin, and I.L. Applebaum. 1964. Industrially acquired porphyria. *Archives of Dermatology* 89:793-7.

8. Zugerman, C. 1990. Chloracne. Clinical manifestations and etiology. *Dermatologic Clinics* 8:209-13.

9. Mukerjee, D. 1998. Health impact of polychlorinated dibenzo-p-dioxins: A critical review. *Journal of the Air & Waste Management Association* 48:157-65.

10. Suskind, R.R. 1985. Chloracne, "the hallmark of dioxin intoxication." *Scandinavian Journal of Work, Environment & Health* 11:165-71.

11. Dunagin, W.G. 1984. Cutaneous signs of systemic toxicity due to dioxins and related chemicals. *Journal of the American Academy of Dermatology* 10:688-700.

12. Tindall, J.P. 1985. Chloracne and chloracnegens. *Journal of the American Academy of Dermatology* 13:539-58.

13. Coenraads, P.J., A. Brouwer, K. Olie, and N.J. Tang. 1994. Chloracne. Some recent issues. *Dermatologic Clinics* 12:569-76.

14. Sweeney, M.H., and P. Mocarelli. 2000. Human health effects after exposure to 2,3,7,8-TCDD. *Food Additives and Contaminations* 17:303-16.

15. Geusau, A., W. Jurecka, H. Nahavandi, J.B. Schmidt, G. Stingl, and E. Tschachler. 2000. Punctate keratoderma-like lesions on the palms and soles in a patient with chloracne: A new clinical manifestation of dioxin intoxication? *British Journal of Dermatology* 143:1067-71.

16. Geusau, A., E. Tschachler, M. Meixner, O. Papke, G. Stingl, and M. McLachlan. 2001. Cutaneous elimination of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *British Journal of Dermatology* 145:938-43.

17. Geusau, A., K. Abraham, K. Geissler, M.O. Sator, G. Stingl, and E. Tschachler. 2001. Severe 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) intoxication: Clinical and laboratory effects. *Environmental Health Perspectives* 109:865-9.

18. Rodriguez-Pichardo, A., F. Camacho, C. Rappe, M. Hansson, A.G. Smith, and J.B. Greig. 1991. Chloracne caused by ingestion of olive oil contaminated with PCDDs and PCDFs. *Human and Experimental Toxicology* 10:311-22.

19. Rodriguez-Pichardo, A., and F. Camacho. 1990. Chloracne as a consequence of a family accident with chlorinated dioxins. *Journal of the American Academy of Dermatology* 22:1121.

20. Doss, M., H. Sauer, R. von Tiepermann, and A.M. Colombi. 1984. Development of chronic hepatic porphyria (porphyria cutanea tarda) with inherited uroporphyrinogen decarboxylase deficiency under exposure to dioxin. *International Journal of Biochemistry* 16:369-73.

21. McConnell, R., K. Anderson, W. Russell, K.E. Anderson, R. Clapp, E.K. Silbergeld, and P.J. Landrigan. 1993. Angiosarcoma, porphyria cutanea tarda, and probable chloracne in a worker exposed to waste oil contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *British Journal of Industrial Medicine* 50:699-703.

22. Signorini, S., P.M. Gerthoux, C. Dassi, M. Cazzaniga, P. Brambilla, N. Vincoli, and P. Mocarelli. 2000. Environmental exposure to dioxin: The Seveso experience. *Andrologia* 32:263-70.

23. Adams, E.M., D.D. Irish, and H.C. Spencer. 1941. The response of rabbit skin to compounds reported to have caused acneiform dermatitis. *Industrial Medicine and Industrial Hygiene* 2:1-4.

24. Jones, E.L., and H. Kizek. 1962. A technique for testing acnegenic potency in rabbits, applied to potent acnegen, 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Investigative Dermatology* 9:511-17.

25. Inagami, K., T. Koga, M. Kikuchi, M. Hashimoto, H. Takahashi, and K. Wada. 1969. Experimental study of hairless mice following administration of rice oil used by a Yusho patient. *Fukuoka Igaku Zasshi* 60:548-53.

26. Puhvel, S.M., M.J. Connor, and M. Sakamoto. 1991. Vitamin A deficiency and the induction of cutaneous toxicity in murine skin by TCDD. *Toxicology and Applied Pharmacology* 107:106-16.

27. Knutson, J.C., and A. Poland. 1982. Response of murine epidermis to 2,3,7,8-tetrachlorodibenzo-p-dioxin: Interaction of the Ah and hr loci. *Cell* 30:225-34.

28. Puhvel, S.M., M. Sakamoto, D.C. Ertl, and R.M. Reisner. 1982. Hairless mice as models for chloracne: A study of cutaneous changes induced by topical application of established chloracnegens. *Toxicology and Applied Pharmacology* 64:492-503.

29. Panteleyev, A.A., R. Paus, W. Ahmad, J.P. Sundberg, and A.M. Christiano. 1998. Molecular and functional aspects of the hairless (hr) gene in laboratory rodents and humans. *Experimental Dermatology* 7:249-67.

30. Panteleyev, A.A., R. Thiel, R. Wanner, J. Zhang, V.S. Roumak, R. Paus, D. Neubert, B.M. Henz, and T. Rosenbach. 1997. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCCD) affects keratin 1 and keratin 17 gene expression and differentially induces keratinization in hairless mouse skin. *Journal of Investigative Dermatology* 108:330-5.

31. McConnell, E.E., J.A. Moore, and D.W. Dalgard. 1978. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rhesus monkeys (Macaca mulatta) following a single oral dose. *Toxicology and Applied Pharmacology* 43:175-87.

32. Mebus, C.A., V.R. Reddy, and W.N. Piper. 1987. Depression of rat testicular 17-hydroxylase and 17,20-lyase after administration of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Biochemical Pharmacology* 36:727-31.

33. Carter, C.D., R.D. Kimbrough, J.A. Liddle, R.E. Cline, M.M. Zack, Jr., W.F. Barthel, R.E. Koehler, and P.E. Phillips. 1975. Tetrachlorodibenzodioxin: An accidental poisoning episode in horse arenas. *Science* 188:738-40.

34. Case, A.A. 1976. Tetrachlorodibenzodioxin (TCDD)—Clinical aspects of poisoning. *Clinical Toxicology* 9:663-7.

35. Birnbaum, L.S., and J. Tuomisto. 2000. Non-carcinogenic effects of TCDD in animals. *Food Additives and Contaminations* 17:275-88.

36. Puhvel, S.M., and M. Sakamoto. 1988. Effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin on murine skin. *Journal of Investigative Dermatology* 90:354-8.

37. Puhvel, S.M., M. Sakamoto, and R.M. Reisner. 1989. Effect of TCDD on the density of Langerhans cells in murine skin. *Toxicology and Applied Pharmacology* 99:72-80.

38. Puhvel, S.M., and M. Sakamoto. 1987. Response of murine epidermal keratinocyte cultures to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD): Comparison of haired and hairless genotypes. *Toxicology and Applied Pharmacology* 89:29-36.

39. Molloy, C.J., M.A. Gallo, and J.D. Laskin. 1987. Alterations in the expression of specific epidermal keratin markers in the hairless mouse by the topical application of the tumor promoters 2,3,7,8-tetrachlorodibenzo-p-dioxin and the phorbol ester 12-O-tetradecanoylphorbol-13-acetate. *Carcinogenesis* 8:1193-9.

40. Greenlee, W.F., R. Osborne, L.G. Hudson, and W.A. Toscano. 1984. Studies on the mechanisms of toxicity of TCDD to human epidermis. In: Biological Mechanisms of Dioxin Action. A. Poland, and R.D. Kimbrough, eds. Cold Spring Harbor Laboratory Press: Cold Spring Harbor, NY.

41. Loertscher, J.A., C.A. Sattler, and B.L. Allen-Hoffmann. 2001. 2,3,7,8-Tetrachlorodibenzo-p-dioxin alters the differentiation pattern of human keratinocytes in organotypic culture. *Toxicology and Applied Pharmacology* 175:121-9.

42. Pazderova-Vejlupkova, J., E. Lukas, M. Nemcova, J. Pickova, and L. Jirasek. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Archives of Environmental Health* 36:5-11.

43. Schecter, A., J.J. Ryan, O. Papke, M. Ball, and A. Lis. 1993. Elevated dioxin levels in the blood of male and female Russian workers with and without chloracne 25 years after phenoxy herbicide exposure: The UFA 'Khimprom' incident. *Chemosphere* 27:253-8.

44. Calvert, G.M., M.H. Sweeney, M.A. Fingerhut, R.W. Hornung, and W.E. Halperin. 1994. Evaluation of porphyria cutanea tarda in U.S. workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *American Journal of Industrial Medicine* 25:559-71.

45. Institute of Medicine. 2003. Veterans and Agent Orange: Update 2002. National Academy Press: Washington, DC.

46. Assennato, G., D. Cervino, E.A. Emmett, G. Longo, and F. Merlo. 1989. Follow-up of subjects who developed chloracne following TCDD exposure at Seveso. *American Journal of Industrial Medicine* 16:119-25.

47. Assennato, G., D. Cervino, and G. Longo. 1987. [Follow-up of patients with chloracne in the Seveso area.] *Giornale Italiano di Medicina del Lavoro ed Ergonomia* 9:15-9.

48. Bertazzi, P.A. 1991. Long-term effects of chemical disasters. Lessons and results from Seveso. *Science of the Total Environment* 106:5-20.

49. Bisanti, L., F. Bonetti, F. Caramaschi, G. Del Corno, C. Favaretti, S.E. Giambelluca, E. Marni, E. Montesarchio, V. Puccinelli, G. Remotti, C. Volpato, E. Zambrelli, and G.M. Fara. 1980. Experiences from the accident of Seveso. *Acta Morphologica Academiae Scientiarum Hungaricae* 28:139-57.

50. Caputo, R., M. Monti, E. Ermacora, G. Carminati, C. Gelmetti, R. Gianotti, E. Gianni, and V. Puccinelli. 1988. Cutaneous manifestations of tetrachlorodibenzo-p-dioxin in children and adolescents. Follow-up 10 years after the Seveso, Italy, accident. *Journal of the American Academy of Dermatology* 19:812-9.

51. Caputo, R. 1989. 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced porphyria cutanea tarda among pediatric patients (letter). *Journal of the American Academy of Dermatology* 21:1321.

52. Caramaschi, F., G. del Corno, C. Favaretti, S.E. Giambelluca, E. Montesarchio, and G.M. Fara. 1981. Chloracne following environmental contamination by TCDD in Seveso, Italy. *International Journal of Epidemiology* 10:135-43.

53. Evans, R.G., K.B. Webb, A.P. Knutsen, S.T. Roodman, D.W. Roberts, J.R., Bagby, W.A. Garrett, Jr., and J.S. Andrews, Jr. 1988. A medical follow-up of the health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Archives of Environmental Health* 43:273-8.

54. Hoffman, R.E., P.A. Stehr-Green, K.B. Webb, R.G. Evans, A.P. Knutsen, W.F. Schramm, J.L. Staake, B.B. Gibson, and K.K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *The Journal of the American Medical Association* 255:2031-8.

55. Mocarelli, P., L.L. Needham, A. Marocchi, D.G. Patterson, Jr., P. Brambilla, P.M. Gerthoux, L. Meazza, and V. Carreri. 1991. Serum concentrations of 2,3,7,8-tetrachlorodibenzo-p-dioxin and test results from selected residents of Seveso, Italy. *Journal of Toxicology and Environmental Health* 32:357-66.

56. Stehr, P.A., G. Stein, K. Webb, W. Schramm, W.B. Gedney, H.D. Donnell, S. Ayres, H. Falk, E. Sampson, and S.J. Smith. 1986. A pilot epidemiologic study of possible health effects associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin contaminations in Missouri. *Archives of Environmental Health* 41:16-22.

57. Stehr-Green, P.A., R.E. Hoffman, K. Webb, R.G. Evans, A.P. Knutsen, W. Schramm, J.L. Staake, B.B. Gibson, and K.K. Steinberg. 1987. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Chemosphere* 16:2089-94.

58. Webb, K.B. 1984. The pilot Missouri health effect study. *Bulletin of Environmental Contamination and Toxicology* 33:662-72.

59. Webb, K., R.G. Evans, P. Stehr, and S.M. Ayres. 1987. Pilot study on health effects of environmental 2,3,7,8-TCDD in Missouri. *American Journal of Industrial Medicine* 11:685-91.

60. Bertazzi, P.A., I. Bernucci, G. Brambilla, D. Consonni, and A.C. Pesatori. 1998. The Seveso studies on early and long-term effects of dioxin exposure: A review. *Environmental Health Perspectives* 106(Suppl 2):625-33.

61. Pesatori, A.C., D. Consonni, S. Bachetti, C. Zocchetti, M. Bonzini, A. Baccarelli, and P.A. Bertazzi. 2003. Short- and long-term morbidity and mortality in the population exposed to dioxin after the "Seveso Accident." *Industrial Health* 41:127-38.

62. Assennato, G., P. Cannatelli, E. Emmett, I. Ghezzi, and F. Merlo, F. 1989. Medical monitoring of dioxin clean-up workers. *American Industrial Hygiene Association Journal* 50:586-92.

63. Beck, H., K. Eckart, W. Mathar, and R. Wittkowski. 1989. Levels of PCDDs and PCDFs in adipose tissue of occupationally exposed workers. *Chemosphere* 18:507-16.

64. Bond, G.G., E.A. McLaren, F.E. Brenner, and R.R. Cook. 1989. Incidence of chloracne among chemical workers potentially exposed to chlorinated dioxins. *Journal of Occupational Medicine* 31:771-4.

65. Bond, G.G., E.A. McLaren, T.E. Lipps, and R.R. Cook. 1989. Update of mortality among chemical workers with potential exposure to the higher chlorinated dioxins. *Journal of Occupational Medicine* 31:121-3.

66. Bond, G.G., R.R. Cook, F.E. Brenner, and E.A. McLaren. 1987. Evaluation of mortality patterns among chemical workers with chloracne. *Chemosphere* 16:2117-21.

67. Calvert, G.M., M.H. Sweeney, M.A. Fingerhut, R.W. Hornung, and W.E. Halperin. 1992. Evaluation of porphyria cutanea tarda and porphyrinuria in dioxin-exposed workers. 12th International Symposium on Dioxins and Related Compounds (Dioxin '92). Finnish Institute of Occupational Health: Helsinki.

68. Cheng, W.N., P.J. Coenraads, Z.H. Hao, and G.F. Liu. 1993. A health survey of workers in the pentachlorophenol section of a chemical manufacturing plant. *American Journal of Industrial Medicine* 24:81-92.

69. Coenraads, P.J., K. Olie, and N.J. Tang. 1999. Blood lipid concentrations of dioxins and dibenzofurans causing chloracne. *British Journal of Dermatology* 141:694-7.

70. Cook, R.R., J.C. Townsend, M.G. Ott,, and L.G. Silverstein. 1980. Mortality experience of employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Journal of Occupational Medicine* 22:530-2.

71. Fitzgerald, E.F., A.L. Weinstein, L.G. Youngblood, S.J. Standfast, and J.M. Melius. 1989. Health effects three years after potential exposure to the toxic contaminants of an electrical transformer fire. *Archives of Environmental Health* 44:214-21.

72. Jansing, P.J., and R. Korff. 1994. Blood levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin and gamma-globulins in a follow-up investigation of employees with chloracne. *Journal of Dermatological Science* 8:91-5.

73. Jones, R.E., and M. Chelsky. 1986. Further discussion concerning porphyria cutanea tarda and TCDD exposure. *Archives of Environmental Health* 41:100-3.

74. Jung, D., J. Konietzko, G. Reill-Konietzko, A. Muttray, H.J. Zimmermann-Holz, M. Doss, H. Beck, L. Edler, and A. Kopp-Schneider. 1994. Porphyrin studies in TCDD-exposed workers. *Archives of Toxicology* 68:595-8.

75. Moses, M., R. Lilis, K.D. Crow, J. Thornton, A. Fischbein, H.A. Anderson, and I.J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *American Journal of Industrial Medicine* 5:161-82.

76. Neuberger, M., W. Landvoigt, and F. Derntl. 1991. Blood levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin in chemical workers after chloracne and in comparison groups. *International Archives of Occupational and Environmental Health* 63:325-7.

77. Neuberger, M., C. Rappe, S. Bergek, H. Cai, M. Hansson, R. Jager, M. Kundi, C.K. Lim, H. Wingfors, and A.G. Smith. 1999. Persistent health effects of dioxin contamination in herbicide production. *Environmental Research* 81:206-14.

78. Neuberger, M., M. Kundi, and R. Jager. 1998. Chloracne and morbidity after dioxin exposure (preliminary results). *Toxicology Letters* 96-97:347-50.

79. Ott, M.G., P. Messerer, and A. Zober. 1993. Assessment of past occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin using blood lipid analyses. *International Archives of Occupational and Environmental Health* 65:1-8.

80. Poland, A.P., D. Smith, G. Metter, and P. Possick. 1971. A health survey of workers in a 2,4-D and 2,4,5-T plan with special attention to chloracne, porphyria cutanea tarda, and psychologic parameters. *Archives of Environmental Health* 22:316-27.

81. Schecter, A., and J.J. Ryan. 1988. Polychlorinated dibenzodioxin and dibenzofuran levels in human adipose tissues from workers 32 years after occupational exposure to 2,3,7,8-TCDD. *Chemosphere* 17:915-20.

82. Von Benner, A., L. Edler, K. Mayer, and A. Zober. 1994. ['Dioxin' investigation program of the chemical industry professional organization.] *Arbeitsmedizin Sozialmedizin Praventivmedizin* 29:11-6.

83. Zober, A., M.G. Ott, and P. Messerer. 1994. Morbidity follow up study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational & Environmental Medicine* 51:479-86.

84. May, G. 1982. Tetrachlorodibenzodioxin: A survey of subjects ten years after exposure. *British Journal of Industrial Medicine* 39:128-35.

85. Zober, A., P. Messerer, and P. Huber. 1990. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. *International Archives of Occupational and Environmental Health* 62:139-57.

86. May, G. 1973. Chloracne from the accidental production of tetrachlorodibenzodioxin. *British Journal of Industrial Medicine* 30:276-83.

87. Sweeney, M.H., G.M. Calvert, G.A. Egeland, M.A. Fingerhut, W.E. Halperin, and L.A. Piacitelli. 1998. Review and update of the results of the NIOSH medical study of workers exposed to chemicals contaminated with 2,3,7,8-tetrachlorodibenzodioxin. *Teratogenesis, Carcinogenesis, and Mutagenesis* 17:241-7.

88. Ryan, J.J., and A. Schecter. 2000. Exposure to Russian phenoxy herbicide producers to dioxin. *Journal of Occupational and Environmental Medicine* 42:861-870.

89. Wendt, A.S. 1985. Iowa Agent Orange survey of Vietnam veterans. Iowa State Department of Health.

90. U.S. Centers for Disease Control. 1988. Health status of Vietnam veterans. II. Physical health. The Centers for Disease Control Vietnam Experience Study. *The Journal of the American Medical Association* 259:2708-14.

91. Stellman, S.D., J.M. Stellman, and J.F. Sommer, Jr. 1988. Health and reproductive outcomes among American Legionnaires in relation to combat and herbicide exposure in Vietnam. *Environmental Research* 47:150-74.

92. Wolfe, W.H., J.E. Michalek, J.C. Miner, A. Rahe, J. Silva, W.F. Thomas, W.D. Grubbs, M.B. Lustik, T.G. Karrison, R.H. Roegner, and D.E. Williams. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. I. Physical health. *The Journal of the American Medical Association* 264:1824-31.

93. Roegner, R.H., W.D. Grubbs, M.B. Lustik, A.S. Brockman, S.C. Henderson, D.E. Williams, W.H. Wolfe, J.E. Michalek, and J.C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

94. Lathrop, G.D., S.G. Machado, T.G. Karrison, W.D. Grubbs, W.F. Thomas, W.H. Wolfe, J.E. Michalek, J.C. Miner, and M.R. Peterson. 1987. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188 262. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

95. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline morbidity study results. NTIS: AD A 138 340. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

96. Burton, J.E., J.E. Michalek, and A.J. Rahe. 1998. Serum dioxin, chloracne, and acne in veterans of Operation Ranch Hand. *Archives of Environmental Health* 53:199-204.

97. Michalek, J.E., B.R. Burnham, H.E. Marden, Jr., J.N. Robinson, V.V. Elequin, J.C. Miner, R.W. Ogershok, W.K. Sneddon, W.D. Grubbs, B.C. Cooper, R.G. Land, V.K. Rocconi, M.E. Yeager, D.E. Williams, and M.E.B. Owens. 2000. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1997 follow-up examination results. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

98. Kim, J.S., H.S. Lim, S.I. Cho, H.K. Cheong, and M.K. Lim. 2003. Impact of Agent Orange exposure among Korean Vietnam veterans. *Industrial Health* 41:149-57.

99. Bodner, K.M., J.J. Collins, L.J. Bloemen, and M.L. Carson. 2003. Cancer risk for chemical workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Occupational and Environmental Medicine* 60:672-75.

100. Institute of Medicine. 1994. Veterans and Agent Orange: Health effects of herbicides used in Vietnam. National Academy Press: Washington, DC.

101. Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L.R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

102. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57:369-78.

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15 CARDIOVASCULAR ASSESSMENT

15.1 INTRODUCTION

15.1.1 Background

15.1.1.1   Organs/Diseases

In the cardiovascular assessment of participants in the Air Force Health Study (AFHS), data regarding cardiac function, vascular cardiac function, and heart disease history were collected based on self-reported information and physical examination. Variables evaluated based on interview data included the lifetime history of essential hypertension, heart disease, myocardial infarction, and stroke or transient ischemic attack. The physical examination included indices of central cardiac function and peripheral vascular function. Assessment of central cardiac function was made by measuring systolic and diastolic blood pressures, heart sounds, and a resting electrocardiograph (ECG). Peripheral vascular function was assessed by presence or absence of carotid bruits, various pulse-point readings, a resting blood pressure index, measures of intermittent claudication and vascular insufficiency, and funduscopic examination of small vessels. Major risk factors for cardiovascular disease include male gender, family history, high blood cholesterol, high blood pressure, diabetes mellitus, cigarette smoking, and physical inactivity (1-3).

15.1.1.2   Toxicology

Animal cardiotoxicology research of dioxin has focused on acute biochemical and functional abnormalities associated with high-level exposure (4). In one study (5), rats were found to have reductions in pulse and blood pressure 6 days after administration of 40 µg/kg of dioxin by gavage and were less responsive to the chronotropic effect of isoproterenol, a beta-agonist. Another study documented changes in myocardial beta-receptors with reduced serum indices of thyroid function and decreased beta-adrenergic responsiveness to isoproterenol in the ventricular papillary muscle of guinea pigs (6). Changes in cardiac function and morphology related to high doses of dioxin also were reported (6, 7). Recently, low doses of dioxin were found to cause myocardial fibrosis in marmosets (4). Other experiments on the effects of dioxin on myocardial contractility in rat (8) and guinea pig (9) atrial muscle, however, have yielded mixed results. Two studies suggested that exposure to dioxin during early chick embryo development was associated with congestive heart failure and increased heart weight (10, 11).

The biochemical effects of dioxin on cardiac muscle were reported in numerous studies. An increase in lipid peroxidation and a decrease in superoxide dismutase activity were noted in the hearts of female rats after dioxin administration (5). Dose-dependent decreases in adipose tissue lipoprotein lipase activity and hepatic low-density lipoprotein binding occurred in rabbits (12) and other laboratory animals (13) in association with elevated serum triglycerides. Other studies documented pre-atherosclerotic lesions in the aortic arch in association with these biochemical abnormalities (12). Dioxin exposure was associated with intravascular thrombosis in rats (7). Two studies provided evidence that the developing vascular endothelium of fish embryos may be a target organ for dioxin toxicity (14, 15).

15.1.1.3   Epidemiology

Epidemiologic studies investigated cardiovascular mortality and morbidity in populations exposed to dioxin through environmental contamination (16-28), occupational exposure (29-57), and in association with service in Southeast Asia (SEA) during the Vietnam War (58-75).

One of the largest human exposures to dioxin occurred as a consequence of an industrial explosion in Seveso, Italy, in 1976 (16-22, 24, 26, 28). In the area closest to the explosion, a median serum dioxin level of 447 parts per trillion (ppt) was measured among residents immediately after the accident (22). In study areas farther away from the accident site, median serum dioxin levels were found to be 94 ppt in a lower-exposed area and 48 ppt in the lowest-exposed area immediately after the accident (22). In the most recent mortality follow-up study of this population through 1996, there was no indication of an increased risk of mortality from all circulatory diseases among residents in the area closest to the explosion (n=804) and in a lower-exposed area (n=5,941) compared to the unexposed population (22). Elevated, but not statistically significant, mortality risks from chronic rheumatic heart disease and hypertension were found among residents in the area closest to the explosion, but not among the populations farther away from the explosion site (22). These findings were similar to earlier mortality follow-up studies of the Seveso population (24, 26). Other studies of environmentally exposed populations also found little indication for a dioxin-related increased risk of cardiovascular disease morbidity or mortality (23, 25, 27).

Cardiovascular mortality and morbidity were evaluated in several worker cohorts occupationally exposed to dioxins in studies conducted by the International Agency for Research on Cancer (IARC) (41, 52) and the National Institute for Occupational Safety and Health (NIOSH) (32, 48), as well as in studies of production workers at Dow Chemical Company (30, 31, 35, 36, 43, 45, 47), Monsanto (34, 42, 49, 54, 55), BASF (44, 46, 50, 56, 57), and in the Netherlands (39), Germany (29, 37, 38, 53), United States (51), and Britain (33, 76). The IARC study included the Dutch, German, and British workers, whereas the NIOSH cohort included workers studied separately in the Dow Chemical Company and Monsanto studies. In addition, a report of Japanese municipal waste incinerator workers was identified (40).

The most recent update of the IARC study evaluated the mortality experience of 21,863 male and female workers exposed to dioxins in 12 countries from 1939 to 1992 (41, 52). No overall increased risk of circulatory system diseases mortality was observed in this cohort compared to national mortality rates (41); however, a more detailed investigation revealed an elevated risk of mortality for all circulatory diseases combined, specifically an elevated risk of mortality for cerebrovascular and ischemic heart disease among those with potential dioxin exposure relative to unexposed workers (52). No consistent patterns with years since first exposure and duration of dioxin exposure were found (52).

Two cohorts included in the IARC study evaluated the risk of cardiovascular disease in relation to serum dioxin levels. In the German study of 1,189 male workers involved in the production of herbicides and insecticides, mortality from circulatory diseases was evaluated from 1952 through 1992 (29, 37, 38). The risk of mortality from cardiovascular disease and ischemic heart disease was highest among workers with the highest estimated exposure to dioxins relative to unexposed workers (38). In a recent update of the Dutch cohort of 1,167 workers from 1955 through 1991, an elevated ischemic heart diseases mortality risk was related to exposure; other circulatory system disease mortality risk was also elevated, but not in an exposure-response manner (39).

As part of the NIOSH Dioxin Registry, cause-specific mortality was initially determined in 5,172 workers exposed to dioxin at 12 U.S. chemical production plants (77). Recent updates of this cohort extended the period of follow-up by 6 years through 1993, and included analyses restricted to 3,538 workers in eight plants for whom qualitative indices of dioxin air levels could be determined and co-exposure to pentachlorophenol could be ruled out (48). Overall mortality from ischemic heart disease in this cohort was elevated and a statistically significant exposure-response relation (Relative Risk [RR] = 1.09, 95% confidence interval: [1.0,1.2]) with cumulative exposure to dioxin was observed (48). In a cross-sectional study of 281 workers and 260 unexposed controls, NIOSH investigators found little evidence of a long-term effect of high dioxin exposure on adverse cardiovascular outcomes; however, serum dioxin

levels were associated with myocardial infarction risk based on self-report or ECG diagnosis (32). Smaller studies of workers at Dow Chemical Company and Monsanto found little evidence of an elevated risk of mortality from circulatory system diseases among workers potentially exposed to dioxins (30, 31, 34-36, 42, 43, 45, 47, 49, 54, 55).

A follow-up study (1953 to 1992) of 243 German factory workers exposed to dioxin during a chemical explosion in 1953 reported that the median serum dioxin levels ranged from 148 ppt among workers without chloracne to 1,118 ppt among those with severe chloracne (46, 56). No exposure-related increase in mortality from diseases of the circulatory system was observed based on a total of 37 cases (46). Furthermore, there was no association between serum dioxin levels and morbidity from disorders of the circulatory system (56). In a small cross-sectional study of 96 Japanese municipal waste incinerator workers potentially exposed to dioxins, no increased risk of hypertension was found (40).

The AFHS is unique among studies that have examined cardiovascular disease in Vietnam veterans because serial serum dioxin data have been incorporated into longitudinal analyses (65, 66, 72-74, 78-82). Previous AFHS examinations showed mixed results with respect to cardiovascular endpoints. In the baseline and 1987 follow-up examinations, manual examination of the pulses revealed an increased prevalence of pulse deficits in the Ranch Hand cohort relative to Comparisons (72, 81). In the 1985 AFHS follow-up examination, which incorporated Doppler peripheral vascular studies into the protocol, no significant group differences were found (82). When the 1987 follow-up examination data were analyzed relative to serum dioxin levels, Ranch Hand participants in the high exposure category had higher percentages of peripheral pulse abnormalities and were at greater risk of developing systemic arterial hypertension relative to Comparisons (78). In contrast, there was a significant reduction in risk of developing heart disease reported historically or verified by medical records review (78). In the 1992 follow-up examination, surviving Ranch Hands were found to be less at risk of developing heart disease over time than Comparisons, and a significant inverse dose-response effect was noted with respect to the body burden of dioxin as measured in 1987 (79). In the 1997 follow-up examination, circulatory disorders, including myocardial infarction and stroke, were unrelated to dioxin levels or exposure categories (80). A modest increase in the prevalence of hypertension was found related to 1987 dioxin levels. Ranch Hand veterans were also more likely to report heart disease, which was not consistently associated with levels of exposure (80).

A recent follow-up report in 1998 evaluating postservice mortality among Ranch Hands (66) found no evidence of an elevated risk of mortality from circulatory diseases in general. Elevated risks, although not statistically significant, were observed for several specific circulatory disorders, such as atherosclerotic heart disease, cerebrovascular disease, hypertensive disease, and other circulatory diseases in Ranch Hand enlisted groundcrew, the subgroup with the highest median dioxin level (66).

The prevalence of hypertension, vasculopathy, and ischemic and valvular heart disease was found to be higher among Korean Vietnam veterans as compared to Korean nonveterans (75). In addition, prevalence of ischemic heart disease was found to be associated with semi-quantitative indicators of Agent Orange exposure based on military region, duration of service, and type and frequency of contact to Agent Orange (75). Other studies of circulatory disease risk among Vietnam veterans have been inconsistent. Some studies reported increased risks among Vietnam veterans (64, 67, 68), while others found no evidence suggesting an elevated risk (61-63, 69-71).

The Institute of Medicine (IOM) concluded that there is "inadequate or insufficient" evidence to establish an association between dioxin exposure and the occurrence of specific circulatory disorders, including coronary artery disease, myocardial infarction, stroke and hypertension, or circulatory diseases in general (83-87).

15.1.2 Summary of Previous Analyses of the Air Force Health Study

15.1.2.1 1982 Baseline Examination Summary Results

The 1982 baseline examination found no statistically significant differences between the Ranch Hand and Comparison groups in systolic or diastolic blood pressures, the frequency of abnormal ECGs, heart sound abnormalities, abnormal funduscopic findings, or carotid bruits. No statistically significant differences were found between the two groups in the occurrence of reported or verified heart disease or heart attacks.

More than 80 percent of the cardiac conditions reported on the study questionnaire were verified by a detailed review of medical records. There was a strong correlation between the past medical history of cardiac disease and the baseline examination cardiovascular findings, although the differences in peripheral pulse abnormalities occurred primarily in older individuals without a history of cardiovascular disease. Finally, the well-known risk factors of age, smoking, and cholesterol were found to be correlated with each other and with several of the cardiovascular response variables.

15.1.2.2 1985 Follow-up Examination Summary Results

The analysis of cardiovascular disease history did not reveal significant group differences in reported or verified hypertension, reported heart disease, or reported or verified heart attacks. There were no group differences in verified heart disease. The verified cardiovascular history and the central and peripheral cardiovascular abnormalities detected at the physical examination were correlated.

In the analyses of peripheral vascular function, no significant overall group differences were observed for abnormalities involving radial, femoral, popliteal, posterior tibial, dorsalis pedis, or three anatomic aggregates of these pulses (leg pulses, peripheral pulses, and all pulses), either by manual palpation or Doppler techniques. This overall finding was in distinct contrast to the 1982 baseline examination, which, by the manual palpation method, showed significant peripheral pulse deficits in Ranch Hands. This reversal in pulse findings over the two examinations may be attributed to the rigid 4-hour tobacco abstinence applied prior to Doppler testing, although other factors may have been involved.

15.1.2.3 1987 Follow-up Examination Summary Results

The assessment of the central cardiac function found the groups to be similar, although significantly fewer Ranch Hands than Comparisons had bradycardia.

For the peripheral vascular function, Ranch Hands had a higher mean or percent abnormal for diastolic blood pressure (continuous form), carotid bruits, femoral pulses, and dorsalis pedis pulses than did Comparisons. No difference between the two groups was detected in the analysis of the discrete form of diastolic blood pressure.

15.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Examination Summary Results

The cardiovascular evaluation found a significant inverse association with verified history of heart disease. In addition, the analyses of categorized dioxin also indicated a decrease in verified history of heart disease for Ranch Hands with the highest dioxin levels relative to Comparisons with background levels. These Ranch Hands had more essential hypertension by history (after removing the variables body fat and cholesterol from the model).

The analyses of the peripheral vascular function variables displayed significantly higher mean levels of diastolic blood pressure for Ranch Hands in the low and high categories than Comparisons (without

adjustment for body fat). Similar to the analysis of systolic blood pressure, the analysis of diastolic blood pressure in its discrete form did not display a significant association with dioxin within the low and high dioxin categories. Ranch Hands generally exhibited a significantly higher risk of absent femoral, dorsalis pedis, and posterior tibial pulses relative to Comparisons. These observations were thought to represent a subclinical effect of dioxin on the cardiovascular system.

15.1.2.5   1992 Follow-up Examination Summary Results

Similar to the 1987 examination, verified heart disease among Ranch Hands decreased significantly with increasing levels of 1987 dioxin. Ranch Hands also displayed an increased history of essential hypertension for increasing levels of 1987 dioxin.

A few other central cardiac function endpoints, including nonspecific ST- and T-wave changes, right bundle branch block (RBBB), and prior ECG evidence of myocardial infarction, displayed significant positive associations with 1987 dioxin; none of these endpoints displayed any group difference between Ranch Hands and Comparisons. These findings, in conjunction with the increase in the number of deaths caused by diseases of the circulatory system for Ranch Hand nonflying enlisted personnel based on the 1994 AFHS mortality update (88), showed potential associations with dioxin.

The analyses of the peripheral vascular function variables displayed significant group differences for the enlisted groundcrew stratum for a few of the pulse endpoints and significant differences between Ranch Hands in the high dioxin category and Comparisons. None of these associations was supported by a significant association with initial or 1987 dioxin. Longitudinal analyses of the pulse endpoints also indicated that Ranch Hands in the enlisted groundcrew stratum and in the high initial dioxin category had a greater prevalence of pulse deficits since the 1985 follow-up examination than Comparisons. Again, these associations were not supported by a significant dose-response effect with initial dioxin.

Overall, the development of cardiovascular disease did not appear to be associated positively with dioxin. Dioxin associations with selected endpoints, as discussed above, together with mortality results, pointed to the need for further evaluation.

15.1.2.6   1997 Follow-up Examination Summary Results

Analyses revealed that Ranch Hands had a significantly higher percentage of participants with a history of heart disease (excluding essential hypertension) than did Comparisons and, in particular, within enlisted flyers. The risk of disease, however, was not significantly increased in Ranch Hand enlisted groundcrew—the military occupation with the highest dioxin levels. The association between heart disease and initial dioxin for Ranch Hands showed a nonsignificant inverse dose-response trend, with heart disease decreasing as initial dioxin increased. Furthermore, Ranch Hands in the background and the low dioxin categories had more heart disease than did Comparisons, but this increase was not seen in Ranch Hands in the high dioxin category. Increases in tachycardia and other ECG findings, such as pre-excitation, were seen for Ranch Hands in the high dioxin category, although the analyses were based on a sparse number of abnormalities. A significant positive association between initial dioxin and evidence of prior myocardial infarction from the ECG was observed in Ranch Hands. A positive association between 1987 dioxin and essential hypertension also was observed in Ranch Hands. In contrast to previous AFHS examinations, no relation was found between peripheral pulses and any measures of exposure.

In contrast to prior examinations, the 1997 follow-up examination documented that Ranch Hands were more likely than Comparisons to have historical evidence for heart disease (excluding essential

hypertension), but were not at greater risk for the occurrence of pulse deficits. By all other indices, the prevalence of cardiovascular disease appeared similar in both cohorts. The verified history of essential hypertension was associated with 1987 dioxin, and the evidence of prior myocardial infarction from the ECG was associated with initial dioxin. These findings, in conjunction with the increase in the number of deaths caused by diseases of the circulatory system for Ranch Hand nonflying enlisted personnel based on the 1994 AFHS mortality update (88), showed associations with dioxin.

15.1.3 Parameters for the 2002 Cardiovascular Assessment

15.1.3.1   Dependent Variables

The analysis of the cardiovascular assessment was based on medical records verification of the data collected from the 2002 questionnaire and data from the 2002 follow-up physical examination. No laboratory examination data were analyzed as cardiovascular dependent variables, although data from the laboratory examination were used as covariates.

15.1.3.1.1 Medical Records Variables

The 2002 questionnaire captured data on the occurrence of heart conditions. Medical records review was accomplished to confirm reported heart conditions and to identify any unreported conditions for each participant that attended the 2002 physical examination. These data from the 2002 physical examination were combined with data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations to form a complete history for essential hypertension, heart disease (excluding essential hypertension), myocardial infarction, and stroke or transient ischemic attack for each participant. Each of these conditions was classified as "yes" or "no" and analyzed. The analyses performed in this chapter were based on the 1,951 participants who attended the 2002 follow-up examination.

International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes were used to classify the four conditions described above. The following ICD-9-CM codes were used: essential hypertension (ICD-9-CM codes 401.0-401.9), heart disease (excluding essential hypertension) (ICD-9-CM codes 391.0-391.9, 392.0-392.9, 393.0-398.99, 402.0-402.91, 404.0-404.93, and 410.0-429.9), myocardial infarction (ICD-9-CM codes 410.0-410.92, and 412), and stroke or transient ischemic attack (ICD-9-CM codes 435.0-436).

A large percentage of participants (approximately 82 percent) were determined to have heart disease. The conditions comprising heart disease were numerous, but the predominate ICD-9-CM codes were ICD-9-CM code 426 (conduction disorders) and ICD-9-CM code 427 (cardiac dysrhythmias).

Participants with a verified heart condition prior to service in SEA were excluded from all analyses. A pre-SEA heart condition did not include pre-SEA essential hypertension. Participants with a verified history of essential hypertension prior to service in SEA were also excluded from the analysis of verified history of essential hypertension.

15.1.3.1.2 Physical Examination Variables

Cardiovascular data obtained from the 2002 physical examination were divided into the following two categories for analysis: central cardiac function and peripheral vascular function.

15.1.3.1.2.1 Central Cardiac Function

The assessment of the central cardiac function at the cardiovascular examination was made by measurements of systolic blood pressure, diastolic blood pressure, heart sounds (by auscultation), and an ECG. Systolic and diastolic blood pressures were determined by a Critikon Dinamap 1846SXP® automated electronic monitor with the nondominant arm placed at heart level; the lowest diastolic pressure and the corresponding systolic pressure of three measurements taken 3 minutes apart were recorded. Detection of abnormal heart sounds was conducted by standard auscultation. Fourth heart sounds were assessed; murmurs were graded in intensity and location and were judged by the examiners to be functional (normal) or organic (abnormal) in nature.

The standard 12-lead (leads I, aVF, and precordial lead V5) ECG was performed and rhythm strips were obtained for all participants. Participants were asked to abstain from tobacco prior to the ECG because of the constrictive arterial effect of nicotine. Standard PR, QRS, and QT intervals were examined, as was the electrical axis. Morphology of the ECG complex was examined using P-waves, Q-waves, U-waves, QRS morphology, and ST-T morphology. Chamber enlargement using standard criteria was assessed. Evidence of a prior myocardial infarction and arrhythmias were noted. Arrhythmias grouped together for analysis included atrial flutter, atrial fibrillation, A-V dissociation, junctional rhythm, multifocal atrial rhythm, and multifocal or unifocal premature beats. Any A-V nodal blocks were categorized as first-, second-, or third-degree. The overall ECG examination was analyzed, as were the following abnormalities: (1) RBBB, (2) left bundle branch block (LBBB), (3) nonspecific ST- and T-wave changes, (4) bradycardia (a resting pulse rate less than 50 beats per minute), (5) tachycardia (a resting pulse rate greater than 100 beats per minute), (6) arrhythmia, (7) evidence of a prior myocardial infarction, and (8) other diagnoses (ventricular aneurysm and Wolff-Parkinson-White syndrome).

Variables analyzed in the evaluation of the central cardiac function included systolic blood pressure, diastolic blood pressure, heart sounds, and the ECG assessments listed above. Both systolic and diastolic blood pressures were analyzed as continuous and discrete variables. Systolic blood pressure was classified as "normal" (≤140 mm Hg) and "abnormal" (>140 mm Hg), and diastolic blood pressure was classified as "normal" (≤90 mm Hg) and "abnormal" (>90 mm Hg). Participants with a verified pre-SEA heart condition were excluded from all analyses of the central cardiac function variables.

15.1.3.1.2.2 Peripheral Vascular Function

The peripheral vascular function was assessed during the cardiovascular examination by funduscopic examination of small vessels; presence or absence of carotid bruits; determination of the radial, femoral, popliteal, dorsalis pedis, and posterior tibial pulses by Doppler techniques; a measure of intermittent claudication and vascular insufficiency based on participant responses in the health questionnaire; a resting blood pressure index; and two hyperemic indices used as measures of intermittent claudication.

The funduscopic examination was conducted with undilated pupils in a standard manner, with emphasis placed on the detection of arteriovenous nicking (a sign of chronic blood pressure elevation), hemorrhages, exudates, papilledema, diabetic retinopathy, disk pallor, and increased cupping. The presence or absence of carotid bruits was assessed by auscultation over both carotid arteries.

The Doppler procedure for examining pulses was a progressive array of measurements designed to determine whether a pulse abnormality existed, where the obstruction was most likely located, and whether it had functional implications. The determination of a pulse abnormality was based on an analysis of recorded Doppler waveform morphology. Pulsatility, systolic forward flow, diastolic reverse flow, and diastolic oscillations were examined.

The funduscopic examination, carotid bruits, and the five pulses were dichotomized as "abnormal" or "normal" (or "presence" or "absence") and analyzed. Pulses were considered abnormal if no arterial flow or a monophasic arterial flow was present on either side. In addition, two pulse indices were constructed from the radial, femoral, popliteal, dorsalis pedis, and posterior tibial pulse measurements as follows:

- Leg pulses: femoral, popliteal, dorsalis pedis, and posterior tibial pulses

- Peripheral pulses: radial, femoral, popliteal, dorsalis pedis, and posterior tibial pulses.

Each of these indices was considered "normal" if all components were normal and "abnormal" if one or more pulses were abnormal.

Three indices of claudication using peripheral blood pressure measurements were analyzed. Right and left brachial (upper arm) blood pressures were taken during the vascular examination using the Doppler technique. An occluding cuff was placed around the participant's arm. The brachial artery was palpated in the antecubital fossa and acoustic gel was applied to the skin over the artery. An arterial signal was found using the Doppler probe and the cuff was then inflated until the arterial signal disappeared. The cuff was slowly deflated while the operator listened to the Doppler for systolic breakthrough.

After brachial pressures were recorded, the right and left supine ankle pressures were measured. The cuff was placed around the participant's ankle with the lower edge just above the malleolus. The Doppler transducer was placed over the posterior tibial and the dorsalis pedis artery and the vessel with the strongest Doppler signal was chosen and the cuff was inflated. The operator listened for systolic breakthrough as the cuff was deflated.

A resting pressure index was calculated from the resting ankle systolic pressure and brachial systolic pressure using the following equation:

$$\text{Resting Pressure Index} = \frac{\text{Ankle Systolic Pressure}}{\text{Maximum Brachial Systolic Pressure}}.$$

In normal subjects, the ankle systolic pressure should be higher than the brachial pressure; therefore, a normal pressure index should be greater than 1.0 in both legs. Abnormally low ankle pressures may indicate severe arterial occlusive disease. Thus, a complete occlusion in a main arterial pathway can result in an abnormal pressure index evidenced as a pressure index less than 1.0 in either leg (note: <0.97 in either leg for this index was judged abnormal per NIOSH recommendation). An index below 0.30 can suggest severe arterial ischemia.

Two reactive hyperemic indices were determined. These indices were assessed from measurements after participant exercise; in particular, active pedal plantarflexion (APP), or toe raises, were used. APP was demonstrated to the participant by the examiner. With the hands on the side of the examination table to provide balance, the participant was instructed to rise on the balls of the feet until the heels were off the ground to a full extension, then lower the heels back to the ground. This procedure was repeated at a steady pace for 2 minutes or until the patient could no longer tolerate the procedure due to pain (indicating claudication) or excessive discomfort. The participant was then instructed to lie down on the examination table immediately after the APP, and post-exercise pressures were obtained at the ankle and the brachial arteries at the site of the highest pressures before exercise. Brachial and ankle pressures were obtained at 1 minute post-exercise and 2 minutes post-exercise.

Two hyperemic pressure indices of claudication were calculated, one at 1 minute post-exercise and one at 2 minutes post-exercise, from the brachial and hyperemic ankle systolic pressures as follows:

$$\text{Hyperemic Pressure Index} = \frac{\text{Hyperemic Ankle Systolic Pressure}}{\text{Brachial Systolic Pressure}}.$$

The brachial systolic pressures at 1 and 2 minutes after exercise were measured in the arm with the maximum resting brachial systolic pressure. A normal test was defined as the return of the lowest ankle index to greater than 1.0 (note: <0.97 for the hyperemic pressure index after either 1 or 2 minutes was judged abnormal per NIOSH recommendation). The magnitude of the decrease in the ankle index and the time taken to return to the resting index were related to the severity of the arterial occlusive disease.

Post-exercise indices should remain at or above 1.0 in participants judged as normal. These indices should return to resting (pre-exercise) levels within 2 minutes after exercise.

Participants with a verified heart condition prior to service in SEA were excluded from the analyses of the peripheral vascular function variables.

15.1.3.1.3   Self-reported Questionnaire Variable

In the 2002 questionnaire, each participant was asked the following questions:

- Do you get a pain in either or both of your legs while walking?

- Does this pain ever begin when you are standing still or sitting?

- Do you get this pain in either or both of your calf muscles?

The self-reported answers were used to detect intermittent claudication and vascular insufficiency (yes, no), which indicate an insufficient oxygen supply to the leg muscles. A participant was judged to have intermittent claudication and vascular insufficiency if he answered "yes" to the first and third questions and "no" to the second question.

15.1.3.2   Covariates

A number of covariates were examined for inclusion in the adjusted analysis of the cardiovascular assessment. Many of these covariates were considered to be classical risk factors for chronic heart disease. Covariates examined included age, race, military occupation, lifetime cigarette smoking history, current cigarette smoking, lifetime alcohol history, current alcohol use, uric acid, body mass index, waist-to-hip ratio, cholesterol, high-density lipoprotein (HDL), cholesterol-HDL ratio, family history of heart disease, family history of heart disease before the age of 45, diabetic class, current use of blood pressure medication (for systolic and diastolic blood pressures determined during the physical examination), and length of exercise prior to peripheral blood pressure measurements (for the hyperemic pressure indices).

Age, race, and military occupation were determined from military records. Lifetime alcohol history was based on information from the 2002 questionnaire and combined with similar information gathered at the 1987, 1992, and 1997 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking pattern changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year. Current alcohol use was defined as the average number of drinks per day during the 2 weeks prior to completing the physical examination.

Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 2002 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

Uric acid, cholesterol, HDL, and the cholesterol-HDL ratio were based on laboratory measurements at the AFHS 2002 follow-up examination.

Body mass index was calculated as weight/(height)^2, where the weight was measured in kilograms and the height was measured in meters at the physical examination (89). For purposes of covariate associations for discrete dependent variables, body fat was dichotomized as "not obese" ($\leq$30 kg/m^2) and "obese" (>30 kg/m^2).

A measurement of each participant's hips and waist (in cm) was taken at the 2002 physical examination. This information was used to construct a waist-to-hip ratio that was used as a covariate for cardiovascular endpoints (90).

Family history of heart disease was defined as "yes" if the participant's mother, father, sister(s), or brother(s) had heart trouble or heart disease and "no" otherwise. Family history of heart disease before the age of 45 was defined as "yes" if the participant's mother, father, sister(s), or brother(s) had heart trouble or heart disease before the age of 45 and "no" otherwise.

Diabetic class was used as a covariate in the analysis of the cardiovascular system for the AFHS 2002 follow-up examination. Diabetes is a known risk factor for cardiovascular disease. In the 2002 questionnaire, a general screening question on diabetes was posed. During the in-person health interview each participant was asked: "Since the date of the last interview, has a doctor told you for the first time that you had diabetes?" Medical records review was accomplished to confirm reported diabetes and to identify any unreported diabetes for each participant that attended the 2002 physical examination. These data from the 2002 physical examination were combined with data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations to form a complete history of diabetes for each participant. Participants with a verified history of diabetes, as diagnosed previously by a physician, were combined with those participants with either

- a 2-hour postprandial glucose level of 200 mg/dL or greater on two separate occasions

- a fasting glucose level of 126 mg/dL or greater on two separate occasions, or

- one 2-hour postprandial glucose measurement $\geq$200 mg/dL and one fasting glucose $\geq$126 mg/dL on two separate occasions,

and classified as "diabetic" for the diabetic class covariate. Those participants not classified as "diabetic," as defined above, but with a 2-hour postprandial glucose level of at least 140 mg/dL or a fasting glucose level of at least 110 mg/dL at the 2002 physical examination, were classified as "impaired." Those participants not classified as "diabetic" or "impaired" as defined above were classified as "normal."

Blood pressure medication (yes, no) was used as a covariate for the adjusted analyses of the systolic blood pressure and diastolic blood pressure variables only. The participant reported this information during the in-person interview on a self-reported form that listed physicians and medications.

Essential hypertension, heart disease excluding essential hypertension, myocardial infarction, and stroke or transient ischemic attack capture a history of a cardiovascular condition rather than the current state of a participant's life at the time of the physical examination. Consequently, to reflect the historical nature of these dependent variables, lifetime alcohol history and lifetime cigarette smoking history were used as covariates, but current alcohol use and current cigarette smoking were not. Lifetime alcohol history and lifetime cigarette smoking history reflect the cumulative lifetime effects of alcohol use and tobacco, respectively, whereas current alcohol use and current cigarette smoking emphasize the short period of time near the date of the physical examination.

15.1.4 Statistical Methods

Table 15-1 summarizes the statistical analysis performed for the 2002 cardiovascular assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, exclusions, and statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 15-1.

Table 15-1. Statistical Analysis for the Cardiovascular Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Essential Hypertension	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Heart Disease (Excluding Essential Hypertension)	MR-V	D	Yes No	(1)	(b)	U:LR,CS A:LR
Myocardial Infarction	MR-V	D	Yes No	(1)	(b)	U:LR,CS A:LR
Stroke or Transient Ischemic Attack	MR-V	D	Yes No	(1)	(b)	U:LR,CS A:LR
Systolic Blood Pressure (mm Hg)	PE	C/D	High: >140 Normal: ≤140	(2)	(b)	U:LR,CS,GLM,TT A:LR,GLM
Diastolic Blood Pressure (mm Hg)	PE	C/D	High: >90 Normal: ≤90	(2)	(b)	U:LR,CS,GLM,TT A:LR,GLM
Heart Sounds	PE	D	Abnormal Normal	(3)	(b)	U:LR,CS A:LR
Overall ECG	PE	D	Abnormal Normal	(3)	(b)	U:LR,CS A:LR
ECG: RBBB	PE	D	Yes No	(3)	(b)	U:LR,CS A:LR
ECG: LBBB	PE	D	Yes No	(3)	(b)	U:LR,CS A:LR
ECG: Nonspecific ST- and T-wave Changes	PE	D	Yes No	(3)	(b)	U:LR,CS A:LR

Table 15-1. *Statistical Analysis for the Cardiovascular Assessment (Continued)*

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
ECG: Bradycardia	PE	D	Yes No	(3)	(b)	U:LR,CS A:LR
ECG: Tachycardia	PE	D	Yes No	(3)	(b)	U:LR,CS A:LR
ECG: Arrhythmia	PE	D	Yes No	(3)	(b)	U:LR,CS A:LR
ECG: Evidence of Prior Myocardial Infarction	PE	D	Yes No	(3)	(b)	U:LR,CS A:LR
ECG: Other Diagnoses	PE	D	Yes No	(3)	(b)	U:LR,CS A:LR
Funduscopic Examination	PE	D	Abnormal Normal	(3)	(b)	U:LR,CS A:LR
Carotid Bruits	PE	D	Present Absent	(3)	(b)	U:LR,CS A:LR
Radial Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR,CS A:LR
Femoral Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR,CS A:LR
Popliteal Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR,CS A:LR
Dorsalis Pedis Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR,CS A:LR
Posterior Tibial Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR,CS A:LR
Leg Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR,CS A:LR
Peripheral Pulses	PE	D	Abnormal Normal	(3)	(b)	U:LR,CS A:LR
Resting Pressure Index	PE	C/D	Low: <0.97 Normal: ≥0.97	(3)	(b)	U:LR,CS,GLM,TT A:LR,GLM
Hyperemic Pressure Index (1 minute post-exercise)	PE	C/D	Low: <0.97 Normal: ≥0.97	(4)	(b)	U:LR,CS,GLM,TT A:LR,GLM
Hyperemic Pressure Index (2 minutes post-exercise)	PE	C/D	Low: <0.97 Normal: ≥0.97	(4)	(b)	U:LR,CS,GLM,TT A:LR,GLM
Intermittent Claudication and Vascular Insufficiency Index	Q-SR	D	Abnormal Normal	(3)	(b)	U:LR,CS A:LR

[a]Covariates:

(1) age, race, military occupation, lifetime cigarette smoking history, lifetime alcohol history, cholesterol, HDL, cholesterol-HDL ratio, uric acid, diabetic class, body mass index, waist-to-hip ratio, family history of heart disease, family history of heart disease before age 45.

(2) age, race, military occupation, lifetime cigarette smoking history, current cigarette smoking, lifetime alcohol history, current alcohol use, cholesterol, HDL, cholesterol-HDL ratio, uric acid, diabetic class, body mass index, waist-to-hip ratio, family history of heart disease, family history of heart disease before age 45, taking blood pressure medication.

(3) age, race, military occupation, lifetime cigarette smoking history, current cigarette smoking, lifetime alcohol history, current alcohol use, cholesterol, HDL, cholesterol-HDL ratio, uric acid, diabetic class, body mass index, waist-to-hip ratio, family history of heart disease, family history of heart disease before age 45.

(4) age, race, military occupation, lifetime cigarette smoking history, current cigarette smoking, lifetime alcohol history, current alcohol use, cholesterol, HDL, cholesterol-HDL ratio, uric acid, diabetic class, body mass index, waist-to-hip ratio, family history of heart disease, family history of heart disease before age 45, time exercised prior to peripheral blood pressure measurements.

[b]Exclusions:

(a) participants with a pre-SEA heart disease, participants with pre-SEA essential hypertension.

(b) participants with a pre-SEA heart disease.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	C/D	Born ≥ 1942 Born < 1942
Race	MIL	D	Black Non-Black
Military Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Lifetime Cigarette Smoking History (pack-years)	Q-SR	C/D	0 >0–10 >10
Current Cigarette Smoking (cigarettes/day)	Q-SR	C/D	Never Former >0–20 >20
Lifetime Alcohol History (drink-years)	Q-SR	C/D	0 >0–40 >40
Current Alcohol Use (2 weeks prior to physical examination) (drinks/day)	Q-SR	C/D	0–1 >1
Uric Acid (mg/dL)	LAB	C/D	≤5.5 >5.5
Body Mass Index (kg/m^2)	PE	C/D	Not Obese: ≤30 Obese: >30
Waist-to-hip Ratio	PE	C/D	>1 ≤1
Cholesterol (mg/dL)	LAB	C/D	0-200 201–239 ≥240
HDL (mg/dL)	LAB	C/D	0–35 >35

Variable (Units)	Data Source	Data Form	Cutpoints
Cholesterol-HDL Ratio	LAB	C/D	0–5 >5
Family History of Heart Disease	Q-SR	D	Yes No
Family History of Heart Disease Before Age 45	Q-SR	D	Yes No
Taking Blood Pressure Medication	Q-SR/MR-V	D	Yes No
Length of Exercise Prior to Peripheral Blood Pressure Measurements (seconds)	PE	C/D	<120 120
Diabetic Class	LAB/MR-V	D	• Diabetic: past history of diabetes, as diagnosed previously by a physician, or $\geq$200 mg/dL 2-hour postprandial glucose on two separate occasions, or $\geq$126 mg/dL fasting glucose on two separate occasions, or one 2-hour postprandial glucose measurement $\geq$200 mg/dL and one fasting glucose $\geq$126 mg/dL on two separate occasions • Impaired: not diabetic; $\geq$140 mg/dL 2-hour postprandial glucose or $\geq$110 mg/dL fasting glucose at the 2002 physical examination • Normal: not diabetic or impaired; <140 mg/dL 2-hour postprandial glucose and <110 mg/dL fasting glucose at the 2002 physical examination

Abbreviations

Data Source:
- LAB: 2002 laboratory results
- MIL: Air Force military records
- MR-V: Medical records (verified)
- PE: 2002 physical examination
- Q-SR: AFHS health questionnaires (self-reported)

Data Form:
- D: Discrete form of dependent variable or covariate
- C/D: Continuous and discrete forms of dependent variable; appropriate form for analysis (either continuous or discrete) of covariate

Statistical Analysis:
- U: Unadjusted analysis
- A: Adjusted analysis

Statistical Methods:
- CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
- GLM: General linear models analysis
- LR: Logistic regression analysis
- TT: Two-sample t-test

Four models were examined for each dependent variable given in Table 15-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for covariates. These covariates are given in Table 15-1. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. In an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-4, the median level of exposure to dioxin was highest for enlisted groundcrew, followed by enlisted flyers, then officers.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the Centers for Disease Control and Prevention (CDC) using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in ppt on a lipid weight basis (91). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2. A statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model to account for body mass index-related differences in elimination rate (92).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. Another category was examined by combining the low and high Ranch Hand categories. This combination is referred to in the tables as the "low plus high Ranch Hand" category. These five categories—Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the four Ranch Hand categories and the dependent variable in the Comparison category was examined. As in Model 2, a statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables. One Ranch Hand without a dioxin measure was excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The term "unadjusted" was used in the text and tables as follows: Models 1 and 4 did not adjust for any covariates. Models 2 and 3 adjusted only for body mass index at the time of the blood measurement for dioxin. The term "adjusted" was used in the text and tables as follows: Models 1 and 4 adjusted for the covariates shown in Table 15-1 unless otherwise specified by a footnote to the table. Models 2 and 3 additionally adjusted only for body mass index at the time of the blood measurement for dioxin.

Table 15-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants that were excluded from analyses is given. As noted in Table 15-2, 52 participants did not provide information for family history of heart disease before age 45. Most of these participants did not know the answer to this question. In an attempt not to exclude a substantial number of participants, a limited version of a stepwise procedure was used. If family history of heart disease before age 45 was not significant ($p>0.05$) for the adjusted analysis of a particular model for a dependent variable, this covariate was excluded from the analysis. Excluding family history of heart disease before age 45 from the model allowed these 52 participants to be included in the analysis of the model and thus increased the sample size. The parameters of the model were then re-estimated; these statistics are shown in the tables in this chapter. Those models for which family history of heart disease before age 45 was deleted as a covariate are noted in a footnote to the table.

Table 15-2. Number of Participants Excluded or with Missing Data for the Cardiovascular Assessment

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Systolic Blood Pressure	DEP	1	0	0	1	1	0
Diastolic Blood Pressure	DEP	1	0	0	1	1	0
Heart Sounds	DEP	1	0	0	1	1	0
Overall ECG	DEP	1	0	0	1	1	0
ECG: RBBB	DEP	1	0	0	1	1	0
ECG: LBBB	DEP	1	0	0	1	1	0
ECG: Nonspecific ST- and T-wave Changes	DEP	1	0	0	1	1	0
ECG: Bradycardia	DEP	1	0	0	1	1	0
ECG: Tachycardia	DEP	1	0	0	1	1	0
ECG: Arrhythmia	DEP	1	0	0	1	1	0
ECG: Evidence of Prior Myocardial Infarction	DEP	1	0	0	1	1	0
Funduscopic Examination	DEP	70	96	41	70	70	96
Carotid Bruits	DEP	1	0	0	1	1	0
Radial Pulses	DEP	2	9	1	2	2	9
Popliteal Pulses	DEP	2	1	2	2	2	1
Dorsalis Pedis Pulses	DEP	2	4	1	2	2	4
Posterior Tibial Pulses	DEP	2	3	2	2	2	3
Leg Pulses	DEP	4	4	3	4	4	4
Peripheral Pulses	DEP	6	12	4	6	6	12
Resting Pressure Index	DEP	4	18	3	4	4	18
Hyperemic Pressure Index (1 minute post-exercise)	DEP	28	50	20	28	28	50

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Hyperemic Pressure Index (2 minutes post-exercise)	DEP	28	48	20	28	28	48
Intermittent Claudication and Vascular Insufficiency Index	DEP	0	2	0	0	0	2
Lifetime Cigarette Smoking History	COV	0	3	0	0	0	3
Current Cigarette Smoking	COV	0	2	0	0	0	2
Lifetime Alcohol History	COV	4	5	3	4	4	5
Current Alcohol Use	COV	0	2	0	0	0	2
Body Mass Index	COV	1	0	0	1	1	0
Waist-to-hip Ratio	COV	1	1	0	1	1	1
Family History of Heart Disease	COV	6	5	4	6	6	5
Family History of Heart Disease Before Age 45	COV	28	24	19	28	28	24
Pre-SEA Essential Hypertension	EXC	10	12	7	10	10	12
Pre-SEA Heart Disease (Excluding Essential Hypertension)	EXC	10	18	6	10	10	18

[a]777 Ranch Hands and 1,174 Comparisons for group.
[b]424 Ranch Hands for initial dioxin; 776 Ranch Hands for 1987 dioxin.
[c]776 Ranch Hands and 1,174 Comparisons for categorized dioxin.

Note: DEP = Dependent variable.
       COV = Covariate.
       EXC = Exclusion.

15.2 RESULTS

15.2.1 Dependent Variable-covariate Associations

The cardiovascular dependent variables were tested for associations with each of the covariates used in the adjusted analyses. The complete results are presented in Table F-7. These associations were pairwise between the dependent variable and the covariate and were not adjusted for any other covariates. A brief summary of the pattern of significant ($p \leq 0.05$) dependent variable-covariate associations is described in the following paragraphs.

Age was significantly associated with all dependent variables except diastolic blood pressure (in the discrete form), LBBB, tachycardia and femoral pulses. Among all discrete dependent variables except radial pulses, there was a significantly higher prevalence of a dependent variable abnormality among older participants. An abnormal radial pulse was more prevalent among younger participants than older participants. The continuous form of diastolic blood pressure, resting pressure index, and the hyperemic pressure indices decreased with increasing age. Systolic blood pressure, however, increased as age increased.

Race was significantly associated with the continuous form of diastolic blood pressure and the resting and hyperemic pressure indices and nonspecific ST- and T-wave changes. Black participants had a significantly higher prevalence of abnormal nonspecific ST- and T-wave changes and had a significantly higher mean diastolic blood pressure than non-Blacks. For the continuous form of the pressure indices, Black participants had a significantly lower mean than non-Black participants.

Military occupation was significantly associated with the prevalence of heart disease (excluding essential hypertension), the discrete form of systolic blood pressure, the overall ECG, and the ECG findings of RBBB, nonspecific ST- and T-wave changes, bradycardia, arrhythmia, and evidence of a prior myocardial infarction. For most of these dependent variables, enlisted groundcrew had the lowest prevalence of an abnormality, which may be due to the age difference between enlisted personnel and officers. The mean systolic blood pressure was lowest and the mean diastolic blood pressure was highest in enlisted groundcrew, which also may be due to the age difference between enlisted personnel and officers.

Significant relations also were found between military occupation and the continuous form of all pressure indices. In each case, officers had the highest mean pressure index, indicating better vascular health, on average. A significant association also was found between military occupation and the discrete form of the hyperemic pressure index (1 minute post-exercise). Enlisted flyers were found to have the highest prevalence of a low hyperemic pressure index at 1 minute after exercise.

Lifetime cigarette smoking history was significantly associated with the prevalence of essential hypertension, myocardial infarction, an abnormal overall ECG, evidence of a prior myocardial infarction from the ECG, and an abnormality of all peripheral vascular function variables from the physical examination except radial pulses. In all cases, the prevalence of an abnormality of the dependent variable increased as lifetime cigarette smoking increased. Lifetime cigarette smoking history also was significantly associated with all pressure indices. The presence of low pressure indices increased with increasing lifetime cigarette smoking, and the indices decreased with increasing smoking. In addition, the continuous form of diastolic blood pressure decreased as lifetime cigarette smoking history increased.

Significant associations were found between current cigarette smoking and the ECG measures of LBBB and tachycardia. The heaviest smokers had a higher prevalence of these ECG abnormalities. Significant associations also was found between current cigarette smoking and the peripheral vascular function variables of funduscopic examination, femoral pulses, popliteal pulses, dorsalis pedis pulses, posterior tibial pulses, leg pulses, peripheral pulses, and the pressure indices. The highest prevalence of these abnormalities also was found in the heavier smokers. The continuous form of systolic blood pressure and all pressure indices decreased as current cigarette smoking increased.

Lifetime alcohol history was significantly associated with essential hypertension, heart sounds, overall ECG, and arrhythmia. For all dependent variables, the prevalence of an abnormality was highest for the heaviest drinkers (in terms of drink-years). Significant associations also were found between lifetime alcohol history and dorsalis pedis pulses, posterior tibial pulses, and leg pulses. The highest prevalence of an abnormal pulse also was seen for the heaviest drinkers. All pressure indices (both continuous and discrete forms) were significantly related to lifetime alcohol history. For the continuous measures, the index decreased as lifetime alcohol history increased. For the discrete measures, low pressure indices were highest for the heaviest drinkers. No dependent variables were significantly related to current alcohol use.

The prevalence of essential hypertension, high systolic blood pressure, an abnormal overall ECG, nonspecific ST- and T-wave changes, and arrhythmia was significantly greater for those participants with

higher uric acid levels. In addition, a significant and positive association was found between uric acid and the continuous form of systolic blood pressure. Significant associations were found between uric acid and the prevalence of an abnormality in all peripheral vascular variables except carotid bruits and radial pulses. In each case, a significantly higher prevalence of abnormalities was found for participants with higher uric acid levels. The continuous form of all pressure indices was significantly and inversely related to uric acid.

The prevalence of essential hypertension, high systolic blood pressure and nonspecific ST- and T-wave changes was significantly higher among obese participants. The continuous form of both systolic and diastolic blood pressure was found to have a significant positive relation with body mass index. The presence of an abnormal posterior tibial pulse was significantly higher for participants who were not obese. A significant inverse association was found between body mass index and the continuous form of hyperemic pressure index 1 minute after exercise.

The waist-to-hip ratio was found to have a significant association with essential hypertension, the overall ECG, nonspecific ST- and T-wave changes, bradycardia, funduscopic examination, posterior tibial pulses, and leg pulses. For all dependent variables except bradycardia, the prevalence was significantly higher in participants with a waist-to-hip ratio greater than 1.0. Both the continuous and discrete forms of systolic blood pressure were significantly related to the waist-to-hip ratio. The prevalence of high systolic blood pressure was greater among participants whose waist-to-hip ratio was greater than 1.0. Similarly, systolic blood pressure was higher among those participants with a greater waist-to-hip ratio. All continuous forms of the pressure indices were found to have significant and inverse relations with the waist-to-hip ratio. The discrete form of both hyperemic pressure indices had a significant association with the waist-to-hip ratio. The presence of a low hyperemic pressure index was higher among participants with a waist-to-hip ratio greater than 1.0.

Cholesterol was significantly associated with essential hypertension, heart disease, and myocardial infarction. The prevalence was highest among participants with the lowest cholesterol levels, which may be the result of cholesterol medication use among those participants with these heart conditions. Similar significant relations, where the highest prevalence of an abnormality was found among participants with the lowest cholesterol levels, were seen with the dependent variables of overall ECG, RBBB, evidence of prior myocardial infarction, funduscopic examination, carotid bruits, dorsalis pedis pulses, leg pulses, and the intermittent claudication and vascular insufficiency index. The continuous form of both systolic and diastolic blood pressure was found to have a significant positive relation with cholesterol. Similarly, the greatest percentage of participants with high diastolic blood pressure was seen among participants with the highest cholesterol levels.

Dependent variables found to have significant associations with HDL were essential hypertension, LBBB, and the continuous form of hyperemic pressure index 1 minute after exercise. A significantly higher percentage of participants with low HDL levels were found to have essential hypertension and LBBB. A significant positive relation between HDL and the hyperemic pressure index 1 minute after exercise was observed.

The prevalence of essential hypertension, heart disease, and myocardial infarction was significantly related to the cholesterol-HDL ratio. For each condition, the prevalence was highest among those participants with a low cholesterol-HDL ratio. The continuous forms of systolic blood pressure and diastolic blood pressure showed a significant positive relation to the cholesterol-HDL ratio. Among the ECG measures, significant associations were found between the cholesterol-HDL ratio and the overall ECG, nonspecific ST- and T-wave changes, and bradycardia. The prevalence of these ECG abnormalities was significantly higher among those participants with a low cholesterol-HDL ratio. In addition, a

significant inverse relation was found between the cholesterol-HDL ratio and the continuous form of the hyperemic pressure index 1 minute after exercise.

Family history of heart disease was significantly associated with essential hypertension, heart disease, and myocardial infarction. The prevalence of essential hypertension, heart disease, and myocardial infarction was significantly higher among participants with a family history of heart disease. Family history of heart disease also was significantly associated with both forms of diastolic blood pressure. Mean diastolic blood pressure was higher among participants with no family history of heart disease. Likewise, the prevalence of high diastolic blood pressure was higher among participants with no family history of heart disease. Among the ECG dependent variables, significant associations were found between family history of heart disease and the overall ECG, nonspecific ST- and T-wave changes, and evidence of a prior myocardial infarction. For all three dependent variables, the prevalence of abnormalities was highest among participants with a family history of heart disease.

The prevalences of a myocardial infarction and nonspecific ST- and T-wave changes were highest among participants with a family history of heart disease before age 45. The peripheral vascular function dependent variables of femoral pulses, popliteal pulses, and posterior tibial pulses were significantly higher among participants with family history of heart disease before age 45. A significantly higher percentage of participants with a family history of heart disease before age 45 were found to have a higher prevalence of a low resting pressure index.

Diabetic class was significantly associated with essential hypertension, heart disease, and myocardial infarction. An increasing prevalence of these heart conditions was found with increasing diabetic impairment. Diabetic class was significantly associated with the discrete form of systolic blood pressure and the continuous form of both systolic and diastolic blood pressure. The prevalence of high systolic blood pressure, as well as mean systolic blood pressure, increased with increasing diabetic impairment. In addition, mean diastolic blood pressure was highest in nondiabetics, followed by glucose-impaired participants and diabetics. With the exception of LBBB and tachycardia, all ECG dependent variables had significant associations with diabetic class. With the exception of bradycardia, the prevalence of abnormalities increased with increasing diabetic impairment. Bradycardia was most prevalent among nondiabetics, followed by glucose-impaired participants and diabetics. All peripheral vascular function dependent variables were significantly related to diabetic class except radial pulses and femoral pulses. In each case, the prevalence of abnormalities increased with increasing diabetic impairment. All pressure indices (both continuous and discrete) and the intermittent claudication and vascular insufficiency index were significantly associated with diabetic class. Decreasing mean pressure indices occurred with increasing diabetic impairment. Similarly, for the discrete forms of the pressure indices, prevalence of low pressure indices was highest among those participants classified as diabetic, followed by glucose-impaired participants and nondiabetics.

Current use of blood pressure medication was significantly associated with diastolic blood pressure in the continuous form. Participants who were not taking blood pressure medication were found to have a significantly higher mean diastolic blood pressure.

Length of exercise prior to peripheral blood pressure measurements was significantly associated with all hyperemic pressure indices. Both the hyperemic pressure indices 1 and 2 minutes after exercise were higher as the length of exercise prior to measurement was greater. When analyzing the discrete form of the hyperemic pressure indices, the highest percentage of a low index was found among those with less than 120 seconds of exercise prior to the blood pressure measurements.

15.2.2   Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 15-1. Dependent variables are grouped into three sections: (1) the questionnaire variables, derived from the questionnaire that was administered in the 2002 follow-up and previous AFHS examinations and verified by a medical records review, (2) variables obtained during the 2002 physical examination, and (3) one variable based on self-reported participant information regarding leg muscle pain.

15.2.2.1   Medical Records Variables

15.2.2.1.1 Essential Hypertension

All Model 1, 2, and 3 unadjusted and adjusted analyses of essential hypertension revealed no significant results (Table 15-3(a–f): p>0.06 for all analyses).

The unadjusted Model 4 analysis showed a significant positive association between essential hypertension and 1987 dioxin (Table 14-3(g): Unadjusted RR=1.18, p<0.001). When adjusted for covariates, the relation was not significant (Table 15-3(h): p=0.088).

Table 15-3. Analysis of Essential Hypertension

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*759*	*412 (54.3)*	*0.93 (0.77,1.11)*	*0.411*
	Comparison	*1,146*	*644 (56.2)*		
Officer	Ranch Hand	298	154 (51.7)	0.79 (0.59,1.06)	0.120
	Comparison	449	258 (57.5)		
Enlisted Flyer	Ranch Hand	131	78 (59.5)	0.96 (0.61,1.52)	0.873
	Comparison	182	110 (60.4)		
Enlisted Groundcrew	Ranch Hand	330	180 (54.5)	1.04 (0.79,1.37)	0.786
	Comparison	515	276 (53.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,885*	*0.92 (0.75,1.13)*	*0.418*
Officer	745	0.74 (0.53,1.02)	0.064
Enlisted Flyer	306	0.96 (0.58,1.58)	0.870
Enlisted Groundcrew	834	1.10 (0.81,1.50)	0.527

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-3. Analysis of Essential Hypertension (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a,b]**	**p-Value**
Low	133	77 (57.9)	1.08 (0.92,1.26)	0.331
Medium	141	79 (56.0)		
High	139	88 (63.3)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
406	1.12 (0.91,1.37)	0.292

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,146	644 (56.2)		
Background RH	345	168 (48.7)	0.89 (0.69,1.14)	0.356
Low RH	202	109 (54.0)	0.87 (0.63,1.19)	0.380
High RH	211	135 (64.0)	1.19 (0.87,1.64)	0.282
Low plus High RH	413	244 (59.1)	1.02 (0.80,1.30)	0.869

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-3. Analysis of Essential Hypertension (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,136		
Background RH	342	0.88 (0.67,1.16)	0.363
Low RH	198	0.74 (0.53,1.04)	0.086
High RH	208	1.32 (0.94,1.87)	0.113
Low plus High RH	406	1.00 (0.77,1.29)	0.986

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

   Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	255	119 (46.7)	1.18 (1.08,1.29)	<0.001**
Medium	249	135 (54.2)		
High	254	158 (62.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value$\leq$0.010).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for $\log_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
748	1.11 (0.98,1.25)	0.088

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.1.2 Heart Disease (Excluding Essential Hypertension)

The unadjusted and adjusted Model 1 analyses of heart disease (excluding essential hypertension) each showed significant group differences for enlisted flyers (Table 15-4(a,b): Unadjusted RR=2.56, p=0.010; Adjusted RR=2.46, p=0.015, respectively). The percentage of Ranch Hand enlisted flyers with heart

disease was 91.6 versus 81.0 percent for the Comparison enlisted flyers. No differences in heart disease were seen between Ranch Hands and Comparisons overall, in officers, or in enlisted groundcrew (p>0.10 for all contrasts).

The Model 3 unadjusted analyses of heart disease revealed a significant difference between Ranch Hands in the background dioxin category and Comparisons (Table 15-4(e): Unadjusted RR=1.50, p=0.019). There were no significant differences in the adjusted analyses (Table 15-4(f): p>0.10 for all analyses).

Both unadjusted and adjusted analyses of Model 2 and Model 4 did not reveal significant findings (Table 15-4(c,d,g,h): p>0.15 for all analyses).

Table 15-4. Analysis of Heart Disease (Excluding Essential Hypertension)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*767*	*644 (84.0)*	*1.22 (0.96,1.56)*	*0.101*
	Comparison	*1,156*	*937 (81.1)*		
Officer	Ranch Hand	302	253 (83.8)	0.86 (0.58,1.29)	0.481
	Comparison	453	388 (85.7)		
Enlisted Flyer	Ranch Hand	131	120 (91.6)	2.56 (1.25,5.26)	0.010**
	Comparison	184	149 (81.0)		
Enlisted Groundcrew	Ranch Hand	334	271 (81.1)	1.28 (0.91,1.80)	0.158
	Comparison	519	400 (77.1)		

**: Statistically significant (p-value≤0.010).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*1.20 (0.94,1.54)*	*0.146*
Officer	752	0.80 (0.53,1.21)	0.291
Enlisted Flyer	308	2.46 (1.19,5.11)	0.015*
Enlisted Groundcrew	842	1.33 (0.94,1.89)	0.112

*: Statistically significant (0.010<p-value≤0.050).

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	116 (85.3)	0.92 (0.76,1.11)	0.405
Medium	142	114 (80.3)		
High	140	114 (81.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
411	1.08 (0.85,1.38)	0.524

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	937 (81.1)		
Background RH	348	299 (85.9)	1.50 (1.07,2.11)	0.019*
Low RH	206	171 (83.0)	1.13 (0.76,1.67)	0.544
High RH	212	173 (81.6)	0.99 (0.68,1.45)	0.963
Low plus High RH	418	344 (82.3)	1.06 (0.79,1.42)	0.710

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	1.33 (0.94,1.89)	0.109
Low RH	202	1.03 (0.68,1.54)	0.904
High RH	209	1.21 (0.81,1.82)	0.346
Low plus High RH	411	1.12 (0.82,1.52)	0.476

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

    Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	219 (85.2)	0.92 (0.81,1.03)	0.152
Medium	253	212 (83.8)		
High	256	212 (82.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
755	0.90 (0.78,1.06)	0.200

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.1.3 Myocardial Infarction

All unadjusted and adjusted analyses of myocardial infarction in Model 1 through Model 4 were nonsignificant (Table 15-5(a–h): p>0.07 for all analyses).

Table 15-5. Analysis of Myocardial Infarction

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*767*	*77 (10.0)*	*0.87 (0.64,1.17)*	*0.339*
	Comparison	*1,156*	*132 (11.4)*		
Officer	Ranch Hand	302	28 (9.3)	0.77 (0.48,1.25)	0.292
	Comparison	453	53 (11.7)		
Enlisted Flyer	Ranch Hand	131	15 (11.5)	0.75 (0.38,1.48)	0.408
	Comparison	184	27 (14.7)		
Enlisted Groundcrew	Ranch Hand	334	34 (10.2)	1.02 (0.65,1.61)	0.939
	Comparison	519	52 (10.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*0.81 (0.59,1.12)*	*0.203*
Officer	752	0.77 (0.46,1.27)	0.307
Enlisted Flyer	308	0.58 (0.28,1.20)	0.140
Enlisted Groundcrew	842	1.01 (0.62,1.65)	0.956

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	12 (8.8)	1.11 (0.88,1.40)	0.392
Medium	142	15 (10.6)		
High	140	15 (10.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 15-5. Analysis of Myocardial Infarction (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
411	1.31 (0.97,1.77)	0.082

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for race because of the sparse number of Black Ranch Hands with a history of a myocardial infarction.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	132 (11.4)		
Background RH	348	34 (9.8)	0.86 (0.58,1.29)	0.469
Low RH	206	18 (8.7)	0.74 (0.44,1.24)	0.249
High RH	212	24 (11.3)	0.97 (0.61,1.54)	0.885
Low plus High RH	418	42 (10.0)	0.85 (0.58,1.22)	0.376

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	0.81 (0.53,1.25)	0.345
Low RH	202	0.60 (0.34,1.04)	0.071
High RH	209	1.04 (0.63,1.74)	0.872
Low plus High RH	411	0.79 (0.53,1.19)	0.260

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-5. Analysis of Myocardial Infarction (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	27 (10.5)	1.02 (0.88,1.19)	0.750
Medium	253	21 (8.3)		
High	256	28 (10.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
755	1.03 (0.85,1.24)	0.778

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.1.4 Stroke or Transient Ischemic Attack

All results from unadjusted and adjusted analyses of stroke or transient ischemic attack in Model 1 through Model 4 were nonsignificant (Table 15-6(a–h): p>0.05 for all analyses).

Table 15-6. Analysis of Stroke or Transient Ischemic Attack

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*767*	*29 (3.8)*	*1.22 (0.74,2.01)*	*0.431*
	Comparison	*1,156*	*36 (3.1)*		
Officer	Ranch Hand	302	13 (4.3)	1.23 (0.58,2.59)	0.589
	Comparison	453	16 (3.5)		
Enlisted Flyer	Ranch Hand	131	6 (4.6)	1.21 (0.40,3.70)	0.733
	Comparison	184	7 (3.8)		
Enlisted Groundcrew	Ranch Hand	334	10 (3.0)	1.20 (0.52,2.77)	0.667
	Comparison	519	13 (2.5)		

Table 15-6. Analysis of Stroke or Transient Ischemic Attack (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*1.39 (0.82,2.34)*	*0.223*
Officer	752	1.30 (0.60,2.80)	0.507
Enlisted Flyer	308	1.48 (0.45,4.81)	0.515
Enlisted Groundcrew	842	1.46 (0.61,3.51)	0.401

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	4 (2.9)	1.09 (0.77,1.56)	0.625
Medium	142	6 (4.2)		
High	140	7 (5.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
411	1.26 (0.78,2.03)	0.336

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-6. Analysis of Stroke or Transient Ischemic Attack (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	36 (3.1)		
Background RH	348	12 (3.4)	1.16 (0.59,2.27)	0.660
Low RH	206	7 (3.4)	1.08 (0.47,2.47)	0.851
High RH	212	10 (4.7)	1.48 (0.72,3.04)	0.287
Low plus High RH	418	17 (4.1)	1.27 (0.70,2.30)	0.435

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	1.21 (0.59,2.45)	0.604
Low RH	202	1.10 (0.47,2.57)	0.828
High RH	209	2.16 (0.98,4.77)	0.057
Low plus High RH	411	1.55 (0.82,2.91)	0.174

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

 Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	7 (2.7)	1.07 (0.85,1.35)	0.545
Medium	253	11 (4.3)		
High	256	11 (4.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 15-6. Analysis of Stroke or Transient Ischemic Attack (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
755	1.04 (0.76,1.44)	0.802

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.2 *Physical Examination Variables – Central Cardiac Function*

15.2.2.2.1 *Systolic Blood Pressure (Continuous)*

Ranch Hand enlisted groundcrew were found to have a significantly lower mean systolic blood pressure than Comparison enlisted groundcrew in the unadjusted analyses of Model 1 (Table 15-7(a): difference of means=-2.4 mm Hg, p=0.045). The adjusted analysis, however, showed no significant difference (p=0.136). All other contrasts in both the unadjusted and adjusted analyses of Model 1 were nonsignificant (Table 15-7(a,b): p>0.06 for all analyses).

The unadjusted Model 3 analyses showed a significant difference between Ranch Hands in the low and high dioxin combined category and Comparisons (Table 15-7(e): difference of means=—2.3 mm Hg, p=0.015). The difference remained significant after adjusting for covariates (Table 15-7(f): difference of adjusted means=-2.3 mm Hg, p=0.022). Ranch Hands in the combined low and high dioxin category had a lower adjusted mean systolic blood pressure (128.2 mm Hg) than Comparisons (130.5 mm Hg). In addition, Ranch Hands in the low dioxin category were found to have a significantly lower mean systolic blood pressure (127.6 mm Hg) than Comparisons in the Model 3 adjusted analyses of systolic blood pressure (Table 15-7(f): difference of adjusted means=-2.9 mm Hg, p=0.025).

All Model 2 and Model 4 unadjusted and adjusted analyses of the continuous form of systolic blood pressure were nonsignificant (Table 15-7(c,d,g,h): p>0.39 for all analyses).

Table 15-7. Analysis of Systolic Blood Pressure (mm Hg) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*766*	*127.8*	*-1.5*	*0.064*
	Comparison	*1,156*	*129.3*		
Officer	Ranch Hand	301	129.1	-0.5	0.687
	Comparison	453	129.6		
Enlisted Flyer	Ranch Hand	131	129.2	-1.5	0.450
	Comparison	184	130.7		
Enlisted Groundcrew	Ranch Hand	334	126.1	-2.4	0.045*
	Comparison	519	128.5		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant $(0.010 < p\text{-value} \le 0.050)$.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*756*	*129.2*	*-1.2*	*0.129*
	Comparison	*1,146*	*130.4*		
Officer	Ranch Hand	299	130.1	-0.6	0.636
	Comparison	453	130.7		
Enlisted Flyer	Ranch Hand	128	129.9	-1.1	0.562
	Comparison	180	131.0		
Enlisted Groundcrew	Ranch Hand	329	127.7	-1.8	0.136
	Comparison	513	129.5		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	136	126.6	126.8	0.011	0.000 (0.005)	0.985
Medium	142	128.7	128.7			
High	140	126.6	126.4			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of systolic blood pressure versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	134	127.3	0.086	0.002 (0.006)	0.680
Medium	140	129.0			
High	137	127.1			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of systolic blood pressure versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.
         Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-7. Analysis of Systolic Blood Pressure (mm Hg) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,156	129.3	129.2		
Background RH	347	128.4	129.0	-0.2	0.852
Low RH	206	127.1	126.9	-2.3	0.074
High RH	212	127.5	126.8	-2.4	0.057
Low plus High RH	418	127.3	126.9	-2.3	0.015*

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,146	130.5		
Background RH	344	130.5	0.0	0.980
Low RH	202	127.6	-2.9	0.025*
High RH	209	128.9	-1.6	0.214
Low plus High RH	411	128.2	-2.3	0.022*

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-7. Analysis of Systolic Blood Pressure (mm Hg) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	256	128.6	<0.001	-0.001 (0.003)	0.652
Medium	253	127.8			
High	256	127.0			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of systolic blood pressure versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	254	128.5	0.070	-0.003 (0.004)	0.393
Medium	250	126.7			
High	251	125.9			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of systolic blood pressure versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.
     Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.2.2 Systolic Blood Pressure (Discrete)

The unadjusted and adjusted Model 1 analyses of the discrete form of systolic blood pressure showed no significant differences between Ranch Hands and Comparisons when examined across all occupations and within each occupation (Table 15-8(a,b): p>0.11 for all analyses). In addition, the unadjusted and adjusted Model 2 analyses showed no significant findings (Table 15-8(c,d): p>0.38 for both analyses).

The unadjusted Model 3 analyses of the discrete form of systolic blood pressure revealed significant differences between Comparisons and Ranch Hands in both the low dioxin category and the combined low and high dioxin category (Table 15-8(e): Unadjusted RR=0.67, p=0.035; Unadjusted RR=0.70, p=0.010, respectively). In both cases, the percentage of participants with high systolic blood pressure was lower for Ranch Hands (19.4% in the low dioxin category; 20.3% in the low and high dioxin categories combined) than for Comparisons (26.0%). After adjusting for covariates, both analyses remained significant (Table 15-8(f): Adjusted RR=0.63, p=0.018 for the low dioxin category contrast; Adjusted RR=0.72, p=0.023 for the low and high dioxin categories combined).

The unadjusted Model 4 results were nonsignificant (Table 15-8(g): p=0.065). After adjusting for covariates, the results became significant and indicated an inverse relation between the 1987 dioxin level and the presence of high systolic blood pressure (Table 15-8(h): Adjusted RR=0.86, p=0.023). The

percentages of participants with high systolic blood pressure in the low, medium, and high 1987 dioxin categories were 26.2, 21.7, and 20.7, respectively.

Table 15-8. Analysis of Systolic Blood Pressure (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*175 (22.8)*	*0.84 (0.68,1.04)*	*0.111*
	Comparison	*1,156*	*301 (26.0)*		
Officer	Ranch Hand	301	78 (25.9)	0.89 (0.64,1.23)	0.480
	Comparison	453	128 (28.3)		
Enlisted Flyer	Ranch Hand	131	30 (22.9)	0.75 (0.45,1.27)	0.286
	Comparison	184	52 (28.3)		
Enlisted Groundcrew	Ranch Hand	334	67 (20.1)	0.83 (0.59,1.16)	0.263
	Comparison	519	121 (23.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*0.87 (0.70,1.08)*	*0.203*
Officer	752	0.89 (0.63,1.24)	0.480
Enlisted Flyer	308	0.76 (0.45,1.30)	0.323
Enlisted Groundcrew	842	0.89 (0.63,1.26)	0.524

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	24 (17.6)	0.94 (0.78,1.12)	0.477
Medium	142	39 (27.5)		
High	140	22 (15.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 15-8. Analysis of Systolic Blood Pressure (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
411	0.91 (0.72,1.13)	0.388

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	301 (26.0)		
Background RH	347	90 (25.9)	1.06 (0.80,1.40)	0.674
Low RH	206	40 (19.4)	0.67 (0.46,0.97)	0.035*
High RH	212	45 (21.2)	0.72 (0.50,1.03)	0.072
Low plus High RH	418	85 (20.3)	0.70 (0.53,0.92)	0.010**

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

  *: Statistically significant ($0.010 < $p-value$\leq 0.050$).
**: Statistically significant (p-value≤ 0.010).

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-8. Analysis of Systolic Blood Pressure (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	1.06 (0.80,1.42)	0.674
Low RH	202	0.63 (0.43,0.92)	0.018*
High RH	209	0.82 (0.56,1.19)	0.289
Low plus High RH	411	0.72 (0.54,0.96)	0.023*

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

      Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	67 (26.2)	0.91 (0.81,1.01)	0.065
Medium	253	55 (21.7)		
High	256	53 (20.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
755	0.86 (0.75,0.98)	0.023*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.2.3 Diastolic Blood Pressure (Continuous)

All Model 1 through Model 4 unadjusted and adjusted analyses of the continuous form of diastolic blood pressure showed no significant results (Table 15-9(a–h): p>0.18 for all analyses).

Table 15-9. Analysis of Diastolic Blood Pressure (mm Hg) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*766*	*74.73*	*-0.29*	*0.517*
	Comparison	*1,156*	*75.02*		
Officer	Ranch Hand	301	73.52	-0.08	0.905
	Comparison	453	73.60		
Enlisted Flyer	Ranch Hand	131	74.65	-0.18	0.869
	Comparison	184	74.83		
Enlisted Groundcrew	Ranch Hand	334	75.85	-0.48	0.481
	Comparison	519	76.33		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*756*	*75.43*	*-0.12*	*0.789*
	Comparison	*1,146*	*75.55*		
Officer	Ranch Hand	299	75.15	0.10	0.888
	Comparison	453	75.05		
Enlisted Flyer	Ranch Hand	128	76.01	-0.14	0.898
	Comparison	180	76.15		
Enlisted Groundcrew	Ranch Hand	329	75.13	-0.30	0.647
	Comparison	513	75.43		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	136	73.57	73.52	0.006	0.021 (0.020)	0.305
Medium	142	76.07	76.05			
High	140	75.61	75.68			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of diastolic blood pressure versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	134	75.86	0.150	-0.013 (0.023)	0.590
Medium	140	77.08			
High	137	76.14			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of diastolic blood pressure versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.
Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,156	75.02	75.02		
Background RH	347	74.27	74.23	-0.79	0.185
Low RH	206	74.47	74.48	-0.54	0.457
High RH	212	75.72	75.75	0.73	0.312
Low plus High RH	418	75.10	75.12	0.10	0.851

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-9. Analysis of Diastolic Blood Pressure (mm Hg) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,146	75.57		
Background RH	344	75.55	-0.02	0.966
Low RH	202	75.36	-0.21	0.767
High RH	209	75.28	-0.29	0.688
Low plus High RH	411	75.32	-0.25	0.643

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented
  because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

       Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	256	74.79	0.002	0.015 (0.012)	0.224
Medium	253	73.59			
High	256	75.78			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of diastolic blood pressure versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	254	75.72	0.141	-0.012 (0.014)	0.406
Medium	250	74.40			
High	251	75.13			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of diastolic blood pressure versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.
         Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.2.4 Diastolic Blood Pressure (Discrete)

All unadjusted and adjusted analyses of the discrete form of diastolic blood pressure were nonsignificant in Models 1, 2, and 4 (Table 15-10(a–d,g,h): p>0.07 for all analyses).

The unadjusted Model 3 analysis of the discrete form of diastolic blood pressure revealed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 15-10(e): Unadjusted RR=1.92, p=0.019). The percentage of participants with high diastolic blood pressure was greater among Ranch Hands in the high dioxin category (9.0%) than Comparisons (4.8%). The difference remained significant after adjusting for covariates (Table 15-10(f): Adjusted RR=1.88, p=0.036).

Table 15-10. Analysis of Diastolic Blood Pressure (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*41 (5.4)*	*1.11 (0.73,1.68)*	*0.619*
	Comparison	*1,156*	*56 (4.8)*		
Officer	Ranch Hand	301	11 (3.7)	0.87 (0.41,1.85)	0.711
	Comparison	453	19 (4.2)		
Enlisted Flyer	Ranch Hand	131	7 (5.3)	0.98 (0.36,2.65)	0.972
	Comparison	184	10 (5.4)		
Enlisted Groundcrew	Ranch Hand	334	23 (6.9)	1.35 (0.76,2.39)	0.308
	Comparison	519	27 (5.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*1.17 (0.76,1.78)*	*0.473*
Officer	752	0.93 (0.43,2.01)	0.857
Enlisted Flyer	308	1.00 (0.36,2.75)	0.998
Enlisted Groundcrew	842	1.41 (0.78,2.54)	0.249

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-10. Analysis of Diastolic Blood Pressure (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) High**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	136	2 (1.5)	1.16 (0.88,1.53)	0.289
Medium	142	15 (10.6)		
High	140	11 (7.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
411	1.18 (0.81,1.72)	0.395

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	56 (4.8)		
Background RH	347	13 (3.7)	0.77 (0.41,1.43)	0.409
Low RH	206	9 (4.4)	0.90 (0.44,1.84)	0.764
High RH	212	19 (9.0)	1.92 (1.11,3.31)	0.019*
Low plus High RH	418	28 (6.7)	1.32 (0.81,2.15)	0.267

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-10. Analysis of Diastolic Blood Pressure (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	0.83 (0.44,1.58)	0.577
Low RH	202	0.96 (0.46,2.02)	0.916
High RH	209	1.88 (1.04,3.39)	0.036*
Low plus High RH	411	1.35 (0.81,2.24)	0.244

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	12 (4.7)	1.19 (0.98,1.44)	0.078
Medium	253	5 (2.0)		
High	256	24 (9.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
755	1.14 (0.89,1.46)	0.306

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.2.5 Heart Sounds

There were no significant findings in the Model 1 through Model 4 unadjusted and adjusted analyses of heart sounds (Table 15-11(a-h): p>0.22 for all analyses).

Table 15-11. Analysis of Heart Sounds

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*53 (6.9)*	*1.17 (0.81,1.70)*	*0.405*
	Comparison	*1,156*	*69 (6.0)*		
Officer	Ranch Hand	301	22 (7.3)	0.91 (0.53,1.59)	0.748
	Comparison	453	36 (7.9)		
Enlisted Flyer	Ranch Hand	131	10 (7.6)	1.82 (0.70,4.74)	0.221
	Comparison	184	8 (4.3)		
Enlisted Groundcrew	Ranch Hand	334	21 (6.3)	1.33 (0.73,2.41)	0.355
	Comparison	519	25 (4.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*1.16 (0.79,1.69)*	*0.457*
Officer	752	0.91 (0.52,1.59)	0.732
Enlisted Flyer	308	1.60 (0.60,4.27)	0.343
Enlisted Groundcrew	842	1.37 (0.74,2.54)	0.316

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	9 (6.6)	1.00 (0.75,1.33)	0.978
Medium	142	11 (7.7)		
High	140	9 (6.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
411	0.97 (0.67,1.40)	0.867

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-11. Analysis of Heart Sounds (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	69 (6.0)		
Background RH	347	23 (6.6)	1.19 (0.73,1.95)	0.481
Low RH	206	14 (6.8)	1.13 (0.62,2.05)	0.687
High RH	212	15 (7.1)	1.13 (0.63,2.03)	0.678
Low plus High RH	418	29 (6.9)	1.13 (0.72,1.78)	0.593

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	1.08 (0.65,1.80)	0.774
Low RH	202	1.11 (0.60,2.05)	0.744
High RH	209	1.38 (0.73,2.59)	0.319
Low plus High RH	411	1.24 (0.77,1.99)	0.377

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

　　　Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	17 (6.6)	1.02 (0.86,1.22)	0.801
Medium	253	16 (6.3)		
High	256	19 (7.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 15-11. Analysis of Heart Sounds (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
755	1.07 (0.86,1.34)	0.526

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.2.6 Overall ECG

All unadjusted and adjusted analyses of the overall assessment of the ECG report in Models 1 through 4 were nonsignificant (Table 15-12(a-h): p>0.06 for all analyses).

Table 15-12. Analysis of Overall ECG

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*276 (36.0)*	*1.03 (0.85,1.24)*	*0.771*
	Comparison	*1,156*	*409 (35.4)*		
Officer	Ranch Hand	301	119 (39.5)	0.96 (0.72,1.30)	0.813
	Comparison	453	183 (40.4)		
Enlisted Flyer	Ranch Hand	131	62 (47.3)	1.46 (0.93,2.30)	0.100
	Comparison	184	70 (38.0)		
Enlisted Groundcrew	Ranch Hand	334	95 (28.4)	0.92 (0.68,1.25)	0.614
	Comparison	519	156 (30.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*1.01 (0.82,1.24)*	*0.900*
Officer	752	0.93 (0.68,1.28)	0.670
Enlisted Flyer	308	1.49 (0.92,2.41)	0.106
Enlisted Groundcrew	842	0.93 (0.67,1.29)	0.653

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-12. Analysis of Overall ECG (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	51 (37.5)	0.86 (0.74,1.01)	0.066
Medium	142	49 (34.5)		
High	140	41 (29.3)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
411	1.05 (0.86,1.29)	0.609

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	409 (35.4)		
Background RH	347	134 (38.6)	1.24 (0.96,1.59)	0.096
Low RH	206	75 (36.4)	1.03 (0.75,1.40)	0.861
High RH	212	66 (31.1)	0.77 (0.56,1.06)	0.110
Low plus High RH	418	141 (33.7)	0.89 (0.70,1.13)	0.333

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-12. Analysis of Overall ECG (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	1.16 (0.88,1.52)	0.298
Low RH	202	0.86 (0.61,1.20)	0.362
High RH	209	0.96 (0.67,1.36)	0.802
Low plus High RH	411	0.91 (0.70,1.17)	0.453

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	92 (35.9)	0.94 (0.86,1.03)	0.204
Medium	253	97 (38.3)		
High	256	86 (33.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
755	0.96 (0.85,1.08)	0.471

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.2.7 ECG: RBBB

All Model 1 through Model 4 unadjusted and adjusted analyses results of RBBB were nonsignificant (Table 15-13(a–h): p>0.14 for all analyses).

Table 15-13. Analysis of ECG: RBBB

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*32 (4.2)*	*1.16 (0.72,1.85)*	*0.545*
	Comparison	*1,156*	*42 (3.6)*		
Officer	Ranch Hand	301	15 (5.0)	1.53 (0.74,3.18)	0.253
	Comparison	453	15 (3.3)		
Enlisted Flyer	Ranch Hand	131	9 (6.9)	1.06 (0.43,2.59)	0.903
	Comparison	184	12 (6.5)		
Enlisted Groundcrew	Ranch Hand	334	8 (2.4)	0.82 (0.35,1.97)	0.664
	Comparison	519	15 (2.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*1.11 (0.68,1.80)*	*0.680*
Officer	752	1.54 (0.72,3.25)	0.263
Enlisted Flyer	308	0.95 (0.37,2.40)	0.910
Enlisted Groundcrew	842	0.82 (0.33,1.99)	0.656

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	3 (2.2)	1.08 (0.72,1.61)	0.715
Medium	142	5 (3.5)		
High	140	5 (3.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 15-13. Analysis of ECG: RBBB (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
411	1.17 (0.69,1.97)	0.567

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for race because of the sparse number of Ranch Hands with RBBB present.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	42 (3.6)		
Background RH	347	19 (5.5)	1.52 (0.87,2.66)	0.142
Low RH	206	5 (2.4)	0.66 (0.26,1.69)	0.388
High RH	212	8 (3.8)	1.05 (0.48,2.27)	0.903
Low plus High RH	418	13 (3.1)	0.84 (0.44,1.59)	0.586

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	1.52 (0.84,2.76)	0.169
Low RH	202	0.56 (0.21,1.46)	0.236
High RH	209	1.03 (0.45,2.35)	0.951
Low plus High RH	411	0.76 (0.39,1.49)	0.429

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-13. Analysis of ECG: RBBB (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
Low	256	14 (5.5)	0.92 (0.74,1.15)	0.472
Medium	253	8 (3.2)		
High	256	10 (3.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
755	0.95 (0.71,1.27)	0.709

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for race because of the sparse number of Ranch Hands with RBBB present.

15.2.2.2.8 ECG: LBBB

All Model 1 through Model 4 analyses, both unadjusted and adjusted, of LBBB were nonsignificant (Table 15-14(a-h): p>0.06 for all analyses).

Table 15-14. Analysis of ECG: LBBB

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*8 (1.0)*	*0.75 (0.32,1.77)*	*0.507*
	Comparison	*1,156*	*16 (1.4)*		
Officer	Ranch Hand	301	1 (0.3)	0.15 (0.02,1.16)	0.069
	Comparison	453	10 (2.2)		
Enlisted Flyer	Ranch Hand	131	3 (2.3)	--	0.141[a]
	Comparison	184	0 (0.0)		
Enlisted Groundcrew	Ranch Hand	334	4 (1.2)	1.04 (0.29,3.70)	0.956
	Comparison	519	6 (1.2)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an LBBB.

--: Results were not presented because of the sparse number of participants with an LBBB.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*0.65 (0.27,1.59)*	*0.337*
Officer	752	0.14 (0.02,1.11)	0.062
Enlisted Flyer	308	--	--
Enlisted Groundcrew	842	0.86 (0.23,3.26)	0.826

--: Results were not presented because of the sparse number of participants with an LBBB.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for race because of the sparse number of participants with LBBB present.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	0 (0.0)	1.28 (0.59,2.76)	0.538
Medium	142	2 (1.4)		
High	140	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 15-14. Analysis of ECG: LBBB (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
411	2.19 (0.49,9.86)	0.271

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for race, military occupation, current alcohol use, or diabetic class because of the sparse number of Ranch Hands with LBBB present.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	16 (1.4)		
Background RH	347	5 (1.4)	1.21 (0.44,3.37)	0.713
Low RH	206	1 (0.5)	0.33 (0.04,2.52)	0.286
High RH	212	2 (0.9)	0.58 (0.13,2.58)	0.477
Low plus High RH	418	3 (0.7)	0.44 (0.12,1.62)	0.218

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-14. Analysis of ECG: LBBB (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	0.92 (0.31,2.74)	0.885
Low RH	202	0.26 (0.03,2.11)	0.207
High RH	209	0.69 (0.14,3.41)	0.651
Low plus High RH	411	0.43 (0.11,1.67)	0.221

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.

Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.

Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.

High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for race because of the sparse number of participants with LBBB present.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	2 (0.8)	0.99 (0.64,1.53)	0.976
Medium	253	4 (1.6)		
High	256	2 (0.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
755	0.84 (0.50,1.44)	0.538

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for race because of the sparse number of Ranch Hands with LBBB present.

15.2.2.2.9 ECG: Nonspecific ST- and T-wave Changes

All Model 1 through Model 4 unadjusted and adjusted analyses of nonspecific ST- and T-wave changes were nonsignificant (Table 15-15(a–h): p>0.14 for all analyses).

Table 15-15. Analysis of ECG: Nonspecific ST- and T-wave Changes

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*180 (23.5)*	*1.01 (0.82,1.26)*	*0.908*
	Comparison	*1,156*	*269 (23.3)*		
Officer	Ranch Hand	301	68 (22.6)	0.87 (0.62,1.22)	0.419
	Comparison	453	114 (25.2)		
Enlisted Flyer	Ranch Hand	131	44 (33.6)	1.43 (0.88,2.34)	0.150
	Comparison	184	48 (26.1)		
Enlisted Groundcrew	Ranch Hand	334	68 (20.4)	0.98 (0.70,1.38)	0.928
	Comparison	519	107 (20.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,864*	*1.02 (0.81,1.28)*	*0.860*
Officer	740	0.89 (0.62,1.27)	0.507
Enlisted Flyer	300	1.48 (0.88,2.48)	0.141
Enlisted Groundcrew	824	0.99 (0.69,1.42)	0.946

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	31 (22.8)	0.95 (0.80,1.14)	0.600
Medium	142	33 (23.2)		
High	140	33 (23.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
411	1.14 (0.91,1.43)	0.246

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	269 (23.3)		
Background RH	347	82 (23.6)	1.12 (0.84,1.50)	0.426
Low RH	206	44 (21.4)	0.87 (0.61,1.25)	0.462
High RH	212	53 (25.0)	1.01 (0.72,1.43)	0.951
Low plus High RH	418	97 (23.2)	0.94 (0.72,1.23)	0.652

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,128		
Background RH	337	1.13 (0.83,1.53)	0.448
Low RH	192	0.79 (0.54,1.16)	0.235
High RH	206	1.12 (0.77,1.64)	0.544
Low plus High RH	398	0.95 (0.71,1.27)	0.719

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	53 (20.7)	1.00 (0.90,1.11)	0.971
Medium	253	63 (24.9)		
High	256	63 (24.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
755	0.95 (0.83,1.09)	0.486

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.2.10 ECG: Bradycardia

The Model 1 and 2 unadjusted and adjusted analyses of bradycardia did not result in significant findings (Table 15-16(a–d): p>0.08 for all analyses).

The unadjusted Model 3 analyses revealed that bradycardia was present in a significantly higher percentage of Ranch Hands in the background dioxin category than in Comparisons (Table 15-16(e): Unadjusted RR=1.69, p=0.034). After covariate adjustment, there were no significant differences (Table 15-16(f): p=0.051).

The unadjusted Model 4 analysis of bradycardia revealed a significant inverse association between the presence of bradycardia and 1987 dioxin (Table 15-16(g): Unadjusted RR=0.80, p=0.024). The percentages of participants with bradycardia in the low, medium, and high 1987 dioxin categories were 8.6, 5.9, and 2.7, respectively. After covariate adjustment, the results became nonsignificant (Table 15-16(h): p=0.202).

Table 15-16. Analysis of ECG: Bradycardia

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*44 (5.7)*	*1.32 (0.87,2.00)*	*0.190*
	Comparison	*1,156*	*51 (4.4)*		
Officer	Ranch Hand	301	24 (8.0)	1.42 (0.80,2.53)	0.229
	Comparison	453	26 (5.7)		
Enlisted Flyer	Ranch Hand	131	8 (6.1)	2.93 (0.86,9.93)	0.085
	Comparison	184	4 (2.2)		
Enlisted Groundcrew	Ranch Hand	334	12 (3.6)	0.88 (0.43,1.82)	0.738
	Comparison	519	21 (4.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*1.43 (0.93,2.18)*	*0.104*
Officer	752	1.52 (0.85,2.73)	0.158
Enlisted Flyer	308	2.78 (0.81,9.55)	0.103
Enlisted Groundcrew	842	1.00 (0.47,2.10)	0.993

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	8 (5.9)	0.83 (0.56,1.24)	0.360
Medium	142	5 (3.5)		
High	140	4 (2.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 15-16. Analysis of ECG: Bradycardia (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
411	1.03 (0.62,1.72)	0.914

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for diabetic class because of the sparse number of Ranch Hands with bradycardia present.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	51 (4.4)		
Background RH	347	27 (7.8)	1.69 (1.04,2.76)	0.034*
Low RH	206	11 (5.3)	1.24 (0.64,2.43)	0.524
High RH	212	6 (2.8)	0.68 (0.29,1.60)	0.374
Low plus High RH	418	17 (4.1)	0.91 (0.51,1.64)	0.760

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-16. Analysis of ECG: Bradycardia (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	1.65 (1.00,2.74)	0.051
Low RH	202	1.39 (0.70,2.76)	0.346
High RH	209	0.88 (0.36,2.16)	0.779
Low plus High RH	411	1.10 (0.60,2.02)	0.754

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

　　　Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	22 (8.6)	0.80 (0.65,0.97)	0.024*
Medium	253	15 (5.9)		
High	256	7 (2.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant ($0.010 < $ p-value $ \leq 0.050$).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
755	0.84 (0.65,1.09)	0.202

[a]Relative risk for a twofold increase in 1987 dioxin.

Note:　Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.2.11 ECG: Tachycardia

The Model 1 through Model 4 analyses of tachycardia, both unadjusted and adjusted, were nonsignificant (Table 15-17(a-h): p>0.13 for all analyses).

Table 15-17. Analysis of ECG: Tachycardia

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*3 (0.4)*	*0.65 (0.17,2.50)*	*0.516*
	Comparison	*1,156*	*7 (0.6)*		
Officer	Ranch Hand	301	0 (0.0)	--	0.999[a]
	Comparison	453	1 (0.2)		
Enlisted Flyer	Ranch Hand	131	0 (0.0)	--	0.999[a]
	Comparison	184	1 (0.5)		
Enlisted Groundcrew	Ranch Hand	334	3 (0.9)	0.93 (0.22,3.92)	0.923
	Comparison	519	5 (1.0)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with tachycardia.

--: Results were not presented because of the sparse number of participants with tachycardia.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*0.67 (0.17,2.68)*	*0.562*
Officer	752	--	--
Enlisted Flyer	308	--	--
Enlisted Groundcrew	842	0.96 (0.22,4.19)	0.954

--: Results were not presented because of the sparse number of participants with tachycardia.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for race because of the sparse number of participants with tachycardia present.

(c) MODEL 2: RANCH HANDS − INITIAL DIOXIN − UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	0 (0.0)	2.60 (0.72,9.44)	0.147
Medium	142	0 (0.0)		
High	140	1 (0.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 15-17. Analysis of ECG: Tachycardia (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
415	5.69 (0.24,134.10)	0.132

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for race, military occupation, current cigarette smoking, current alcohol use, the cholesterol-HDL ratio, diabetic class, the waist-to-hip ratio, and family history of heart disease because of the sparse number of Ranch Hands with tachycardia present.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	7 (0.6)		
Background RH	347	2 (0.6)	0.92 (0.19,4.51)	0.920
Low RH	206	0 (0.0)	--	0.555
High RH	212	1 (0.5)	0.80 (0.10,6.59)	0.836
Low plus High RH	418	1 (0.2)	--	0.616

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with tachycardia.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-17. Analysis of ECG: Tachycardia (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	1.22 (0.23,6.52)	0.815
Low RH	202	--	--
High RH	209	0.52 (0.06,4.54)	0.556
Low plus High RH	411	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with tachycardia.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

    Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

    Results were not adjusted for race because of the sparse number of participants with tachycardia present.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	1 (0.4)	1.15 (0.58,2.28)	0.686
Medium	253	1 (0.4)		
High	256	1 (0.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
761	0.79 (0.36,1.76)	0.570

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

    Results were not adjusted for race, military occupation, current cigarette smoking, diabetic class, and family history of heart disease because of the sparse number of Ranch Hands with tachycardia present.

15.2.2.2.12 ECG: Arrhythmia

All Model 1 and Model 4 unadjusted and adjusted analyses of arrhythmia were nonsignificant (Table 15-18(a,b,g,h): p>0.19 for all analyses).

The unadjusted Model 2 analyses revealed a significant inverse relation between initial dioxin and the presence of arrhythmia (Table 15-18(c): Unadjusted RR=0.63, p=0.001). After adjustment for covariates, the relation was not significant (Table 15-18(d): p=0.092).

In the unadjusted analyses of Model 3, a significantly lower percentage of Ranch Hands in the high dioxin category displayed the presence of arrhythmia relative to Comparisons (Table 15-18(e): Unadjusted RR=0.49, p=0.019). After adjustment for covariates, all results were nonsignificant (Table 15-18(f): p≥0.15 for all analyses).

Table 15-18. Analysis of ECG: Arrhythmia

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*73 (9.5)*	*0.87 (0.64,1.18)*	*0.363*
	Comparison	*1,156*	*125 (10.8)*		
Officer	Ranch Hand	301	39 (13.0)	0.98 (0.63,1.50)	0.909
	Comparison	453	60 (13.2)		
Enlisted Flyer	Ranch Hand	131	10 (7.6)	0.61 (0.28,1.33)	0.214
	Comparison	184	22 (12.0)		
Enlisted Groundcrew	Ranch Hand	334	24 (7.2)	0.86 (0.51,1.44)	0.560
	Comparison	519	43 (8.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*0.86 (0.63,1.19)*	*0.362*
Officer	752	0.96 (0.61,1.50)	0.854
Enlisted Flyer	308	0.59 (0.26,1.31)	0.196
Enlisted Groundcrew	842	0.89 (0.52,1.52)	0.668

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-18. Analysis of ECG: Arrhythmia (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	21 (15.4)	0.63 (0.46,0.85)	0.001**
Medium	142	10 (7.0)		
High	140	7 (5.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
411	0.74 (0.51,1.06)	0.092

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	125 (10.8)		
Background RH	347	34 (9.8)	0.98 (0.66,1.47)	0.941
Low RH	206	25 (12.1)	1.11 (0.70,1.76)	0.649
High RH	212	13 (6.1)	0.49 (0.27,0.89)	0.019*
Low plus High RH	418	38 (9.1)	0.73 (0.49,1.10)	0.131

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-18. Analysis of ECG: Arrhythmia (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	0.88 (0.58,1.35)	0.563
Low RH	202	1.03 (0.64,1.67)	0.891
High RH	209	0.63 (0.34,1.18)	0.150
Low plus High RH	411	0.80 (0.53,1.22)	0.309

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	25 (9.8)	0.91 (0.78,1.06)	0.210
Medium	253	30 (11.9)		
High	256	17 (6.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
755	0.89 (0.73,1.08)	0.230

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.2.13 ECG: Evidence of Prior Myocardial Infarction

All unadjusted and adjusted analyses of prior myocardial infarction from the ECG showed no significant results in Model 1 through Model 4 (Table 15-19(a-h): p>0.07 for all analyses).

Table 15-19. Analysis of ECG: Evidence of Prior Myocardial Infarction

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*34 (4.4)*	*0.83 (0.54,1.28)*	*0.404*
	Comparison	*1,156*	*61 (5.3)*		
Officer	Ranch Hand	301	18 (6.0)	1.00 (0.54,1.86)	0.991
	Comparison	453	27 (6.0)		
Enlisted Flyer	Ranch Hand	131	7 (5.3)	0.64 (0.25,1.61)	0.338
	Comparison	184	15 (8.2)		
Enlisted Groundcrew	Ranch Hand	334	9 (2.7)	0.73 (0.33,1.63)	0.441
	Comparison	519	19 (3.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*0.80 (0.51,1.26)*	*0.331*
Officer	752	1.05 (0.55,1.98)	0.886
Enlisted Flyer	308	0.54 (0.21,1.40)	0.201
Enlisted Groundcrew	842	0.71 (0.31,1.63)	0.416

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS − INITIAL DIOXIN − UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	5 (3.7)	1.01 (0.71,1.44)	0.965
Medium	142	8 (5.6)		
High	140	5 (3.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
411	1.57 (0.96,2.59)	0.071

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for race because of the sparse number of Ranch Hands with evidence from the ECG of a prior myocardial infarction.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	61 (5.3)		
Background RH	347	16 (4.6)	0.90 (0.51,1.60)	0.730
Low RH	206	10 (4.9)	0.91 (0.46,1.80)	0.778
High RH	212	8 (3.8)	0.68 (0.32,1.44)	0.312
Low plus High RH	418	18 (4.3)	0.78 (0.45,1.35)	0.374

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	0.81 (0.45,1.47)	0.487
Low RH	202	0.75 (0.37,1.52)	0.422
High RH	209	0.82 (0.37,1.84)	0.632
Low plus High RH	411	0.78 (0.44,1.39)	0.406

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	13 (5.1)	0.97 (0.79,1.21)	0.815
Medium	253	9 (3.6)		
High	256	12 (4.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
755	1.20 (0.88,1.64)	0.252

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.2.14 ECG: Other Diagnoses

One participant had an "other" ECG diagnosis, which was an anteroseptal aneurysm. This participant was a non-Black Ranch Hand enlisted groundcrew. Because only one participant had this condition, statistical analysis was not possible.

15.2.2.3 Physical Examination Variables – Peripheral Vascular Function

15.2.2.3.1 Funduscopic Examination

The Model 1 through Model 4 unadjusted and adjusted analyses of the funduscopic examination were nonsignificant (Table 15-20(a-h): p≥0.11 for all analyses).

Table 15-20. Analysis of Funduscopic Examination

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*698*	*80 (11.5)*	*1.16 (0.85,1.57)*	*0.354*
	Comparison	*1,063*	*107 (10.1)*		
Officer	Ranch Hand	269	25 (9.3)	1.08 (0.63,1.84)	0.789
	Comparison	414	36 (8.7)		
Enlisted Flyer	Ranch Hand	119	16 (13.4)	1.09 (0.55,2.20)	0.799
	Comparison	169	21 (12.4)		
Enlisted Groundcrew	Ranch Hand	310	39 (12.6)	1.24 (0.79,1.93)	0.348
	Comparison	480	50 (10.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,745*	*1.24 (0.89,1.73)*	*0.202*
Officer	682	1.06 (0.60,1.85)	0.851
Enlisted Flyer	283	1.09 (0.52,2.29)	0.815
Enlisted Groundcrew	780	1.49 (0.91,2.43)	0.111

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	119	13 (10.9)	1.07 (0.85,1.35)	0.546
Medium	129	16 (12.4)		
High	129	17 (13.2)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 15-20. Analysis of Funduscopic Examination (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
371	1.09 (0.80,1.47)	0.590

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,063	107 (10.1)		
Background RH	320	34 (10.6)	1.17 (0.78,1.77)	0.448
Low RH	182	22 (12.1)	1.21 (0.74,1.98)	0.450
High RH	195	24 (12.3)	1.15 (0.71,1.86)	0.562
Low plus High RH	377	46 (12.2)	1.18 (0.81,1.71)	0.384

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,055		
Background RH	318	1.44 (0.92,2.26)	0.110
Low RH	179	1.07 (0.63,1.83)	0.801
High RH	192	1.23 (0.72,2.08)	0.446
Low plus High RH	371	1.15 (0.77,1.72)	0.498

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

      Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-20. Analysis of Funduscopic Examination (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	238	20 (8.4)	1.10 (0.96,1.27)	0.172
Medium	224	30 (13.4)		
High	235	30 (12.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
	Adjusted Relative Risk	
n	(95% C.I.)[a]	p-Value
689	1.03 (0.85,1.24)	0.774

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.2 Carotid Bruits

All Model 1 through Model 4 unadjusted and adjusted analyses of carotid bruits were nonsignificant (Table 15-21(a-h): p>0.07).

Table 15-21. Analysis of Carotid Bruits

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*766*	*15 (2.0)*	*0.78 (0.41,1.46)*	*0.425*
	Comparison	*1,156*	*29 (2.5)*		
Officer	Ranch Hand	301	6 (2.0)	0.52 (0.20,1.34)	0.176
	Comparison	453	17 (3.8)		
Enlisted Flyer	Ranch Hand	131	3 (2.3)	1.05 (0.23,4.79)	0.945
	Comparison	184	4 (2.2)		
Enlisted Groundcrew	Ranch Hand	334	6 (1.8)	1.17 (0.40,3.40)	0.775
	Comparison	519	8 (1.5)		

Table 15-21. Analysis of Carotid Bruits (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*0.76 (0.40,1.48)*	*0.418*
Officer	752	0.48 (0.18,1.26)	0.136
Enlisted Flyer	308	1.11 (0.21,5.81)	0.903
Enlisted Groundcrew	842	1.33 (0.43,4.09)	0.624

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	0 (0.0)	1.26 (0.69,2.31)	0.454
Medium	142	3 (2.1)		
High	140	2 (1.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
415	2.34 (0.86,6.38)	0.079

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for diabetic class or family history of heart disease because of the sparse number of Ranch Hands with a carotid bruit present.

Table 15-21. Analysis of Carotid Bruits (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	29 (2.5)		
Background RH	347	9 (2.6)	1.07 (0.50,2.29)	0.865
Low RH	206	2 (1.0)	0.38 (0.09,1.60)	0.186
High RH	212	3 (1.4)	0.54 (0.16,1.80)	0.318
Low plus High RH	418	5 (1.2)	0.45 (0.17,1.20)	0.111

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	0.95 (0.42,2.12)	0.895
Low RH	202	0.33 (0.08,1.45)	0.143
High RH	209	0.77 (0.22,2.76)	0.693
Low plus High RH	411	0.51 (0.19,1.41)	0.194

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	7 (2.7)	0.85 (0.61,1.20)	0.355
Medium	253	3 (1.2)		
High	256	4 (1.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 15-21. Analysis of Carotid Bruits (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
755	0.74 (0.48,1.15)	0.186

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.3 Radial Pulses

All unadjusted and adjusted analyses of radial pulses for Model 1 through Model 4 were nonsignificant (Table 15-22(a-h): p>0.08 for all analyses).

Table 15-22. Analysis of Radial Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*765*	*48 (6.3)*	*0.87 (0.60,1.26)*	*0.458*
	Comparison	*1,148*	*82 (7.1)*		
Officer	Ranch Hand	300	22 (7.3)	1.03 (0.59,1.81)	0.915
	Comparison	449	32 (7.1)		
Enlisted Flyer	Ranch Hand	131	4 (3.1)	0.45 (0.14,1.42)	0.171
	Comparison	182	12 (6.6)		
Enlisted Groundcrew	Ranch Hand	334	22 (6.6)	0.89 (0.52,1.53)	0.671
	Comparison	517	38 (7.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,892*	*0.91 (0.62,1.32)*	*0.602*
Officer	746	1.09 (0.62,1.93)	0.760
Enlisted Flyer	306	0.47 (0.15,1.50)	0.201
Enlisted Groundcrew	840	0.90 (0.52,1.56)	0.710

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-22. Analysis of Radial Pulses (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	135	5 (3.7)	1.32 (0.97,1.79)	0.086
Medium	142	6 (4.2)		
High	140	10 (7.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
410	1.18 (0.78,1.78)	0.443

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Results were not adjusted for race because of the sparse number of Black Ranch Hands with an abnormal radial pulse.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,148	82 (7.1)		
Background RH	347	27 (7.8)	1.12 (0.71,1.77)	0.619
Low RH	205	8 (3.9)	0.52 (0.25,1.10)	0.089
High RH	212	13 (6.1)	0.83 (0.45,1.53)	0.552
Low plus High RH	417	21 (5.0)	0.66 (0.40,1.10)	0.110

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-22. Analysis of Radial Pulses (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,138		
Background RH	343	1.19 (0.74,1.91)	0.470
Low RH	201	0.55 (0.26,1.17)	0.120
High RH	209	0.78 (0.41,1.47)	0.447
Low plus High RH	410	0.66 (0.39,1.10)	0.112

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	20 (7.8)	1.02 (0.85,1.22)	0.871
Medium	252	13 (5.2)		
High	256	15 (5.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
753	1.03 (0.81,1.30)	0.828

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.4 Femoral Pulses

The analyses of Models 1, 2, and 4 did not reveal significant findings for femoral pulses, either unadjusted or adjusted for covariates (Table 15-23(a-d,g,h): p>0.06).

The unadjusted Model 3 analyses revealed a significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 15-24(e): Unadjusted RR=3.15, p=0.041). The adjusted analysis was nonsignificant (Table 15-23(f): p=0.140). No other Model 3 contrasts were significant (Table 15-23(e,f): p>0.08 for all analyses).

Table 15-23. Analysis of Femoral Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*767*	*13 (1.7)*	*2.20 (0.93,5.17)*	*0.068*
	Comparison	*1,156*	*9 (0.8)*		
Officer	Ranch Hand	302	4 (1.3)	1.20 (0.32,4.52)	0.785
	Comparison	453	5 (1.1)		
Enlisted Flyer	Ranch Hand	131	4 (3.1)	2.87 (0.52,15.89)	0.228
	Comparison	184	2 (1.1)		
Enlisted Groundcrew	Ranch Hand	334	5 (1.5)	3.93 (0.76,20.37)	0.103
	Comparison	519	2 (0.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,864*	*1.91 (0.72,5.10)*	*0.193*
Officer	740	1.02 (0.25,4.22)	0.974
Enlisted Flyer	300	6.47 (0.63,66.27)	0.115
Enlisted Groundcrew	824	2.17 (0.34,13.80)	0.411

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	3 (2.2)	0.75 (0.42,1.36)	0.327
Medium	142	2 (1.4)		
High	140	3 (2.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 15-23. Analysis of Femoral Pulses (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
411	0.84 (0.37,1.91)	0.681

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,156	9 (0.8)		
Background RH	348	4 (1.1)	1.51 (0.46,4.98)	0.496
Low RH	206	5 (2.4)	3.15 (1.05,9.51)	0.041*
High RH	212	3 (1.4)	1.79 (0.48,6.72)	0.385
Low plus High RH	418	8 (1.9)	2.37 (0.89,6.32)	0.085

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,128		
Background RH	337	0.91 (0.21,3.90)	0.897
Low RH	192	2.69 (0.72,10.01)	0.140
High RH	206	2.74 (0.59,12.87)	0.200
Low plus High RH	398	2.72 (0.86,8.62)	0.090

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-23. Analysis of Femoral Pulses (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	3 (1.2)	0.91 (0.63,1.31)	0.609
Medium	253	4 (1.6)		
High	256	5 (2.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
755	0.94 (0.58,1.52)	0.797

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.5 Popliteal Pulses

All Model 1 through Model 4 analyses of popliteal pulses, both unadjusted and adjusted, were nonsignificant (Table 15-24(a-h): p>0.19 for all analyses).

Table 15-24. Analysis of Popliteal Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*765*	*18 (2.4)*	*0.90 (0.50,1.63)*	*0.736*
	Comparison	*1,155*	*30 (2.6)*		
Officer	Ranch Hand	301	7 (2.3)	0.70 (0.28,1.73)	0.433
	Comparison	453	15 (3.3)		
Enlisted Flyer	Ranch Hand	130	5 (3.8)	1.01 (0.31,3.26)	0.985
	Comparison	184	7 (3.8)		
Enlisted Groundcrew	Ranch Hand	334	6 (1.8)	1.17 (0.40,3.39)	0.778
	Comparison	518	8 (1.5)		

Table 15-24. Analysis of Popliteal Pulses (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,861*	*0.79 (0.40,1.55)*	*0.482*
Officer	739	0.64 (0.24,1.70)	0.374
Enlisted Flyer	299	1.18 (0.30,4.68)	0.811
Enlisted Groundcrew	823	0.80 (0.22,2.91)	0.731

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	135	4 (3.0)	0.81 (0.50,1.33)	0.395
Medium	142	2 (1.4)		
High	139	5 (3.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
409	0.88 (0.45,1.70)	0.694

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-24. Analysis of Popliteal Pulses (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,155	30 (2.6)		
Background RH	348	6 (1.7)	0.68 (0.28,1.66)	0.398
Low RH	205	6 (2.9)	1.12 (0.46,2.73)	0.802
High RH	211	5 (2.4)	0.88 (0.34,2.31)	0.798
Low plus High RH	416	11 (2.6)	0.99 (0.49,2.01)	0.983

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,127		
Background RH	337	0.50 (0.18,1.42)	0.193
Low RH	191	0.82 (0.29,2.33)	0.712
High RH	205	1.14 (0.38,3.46)	0.812
Low plus High RH	396	0.98 (0.43,2.20)	0.952

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	4 (1.6)	1.03 (0.76,1.38)	0.864
Medium	252	6 (2.4)		
High	255	7 (2.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 15-24. Analysis of Popliteal Pulses (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log_2 (1987 Dioxin) | |
| | **Adjusted Relative Risk** | |
n	**(95% C.I.)[a]**	**p-Value**
753	0.99 (0.66,1.48)	0.954

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.6 Dorsalis Pedis Pulses

All Model 1 through Model 4 unadjusted and adjusted analyses of dorsalis pedis pulses were nonsignificant (Table 15-25(a–h): p>0.27 for all analyses).

Table 15-25. Analysis of Dorsalis Pedis Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*765*	*61 (8.0)*	*0.95 (0.68,1.33)*	*0.778*
	Comparison	*1,152*	*96 (8.3)*		
Officer	Ranch Hand	300	24 (8.0)	0.78 (0.47,1.32)	0.359
	Comparison	451	45 (10.0)		
Enlisted Flyer	Ranch Hand	131	10 (7.6)	0.76 (0.34,1.70)	0.501
	Comparison	183	18 (9.8)		
Enlisted Groundcrew	Ranch Hand	334	27 (8.1)	1.29 (0.76,2.19)	0.341
	Comparison	518	33 (6.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,897*	*0.96 (0.67,1.38)*	*0.841*
Officer	748	0.81 (0.46,1.40)	0.442
Enlisted Flyer	308	0.68 (0.29,1.61)	0.386
Enlisted Groundcrew	841	1.37 (0.78,2.42)	0.275

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-25. Analysis of Dorsalis Pedis Pulses (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Abnormal**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	135	13 (9.6)	1.06 (0.82,1.37)	0.658
Medium	142	7 (4.9)		
High	140	15 (10.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
410	1.14 (0.82,1.58)	0.430

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	**n**	**Number (%) Abnormal**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Comparison	1,152	96 (8.3)		
Background RH	347	25 (7.2)	0.89 (0.56,1.41)	0.623
Low RH	205	16 (7.8)	0.92 (0.53,1.60)	0.771
High RH	212	19 (9.0)	1.04 (0.62,1.75)	0.877
Low plus High RH	417	35 (8.4)	0.98 (0.65,1.47)	0.926

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-25. Analysis of Dorsalis Pedis Pulses (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,143		
Background RH	343	0.87 (0.53,1.43)	0.582
Low RH	201	0.83 (0.46,1.49)	0.522
High RH	209	1.28 (0.72,2.28)	0.409
Low plus High RH	410	1.03 (0.66,1.60)	0.893

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

    Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	16 (6.3)	1.06 (0.90,1.25)	0.455
Medium	252	23 (9.1)		
High	256	21 (8.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
753	1.05 (0.85,1.29)	0.646

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.7 Posterior Tibial Pulses

All unadjusted Model 1 analyses of posterior tibial pulses were nonsignificant (Table 15-26(a): p>0.06 for all analyses). When adjusted for covariates, a significant difference in the presence of abnormal posterior tibial pulses was found overall between Ranch Hands and Comparisons (Table 15-26(b): Adjusted RR=0.59, p=0.027). The Ranch Hand group had 4.3 percent with an abnormal posterior tibial

pulse, whereas the Comparison group had 5.9 percent abnormal. In addition, the presence of abnormal posterior tibial pulses was found in a significantly lower percentage of Ranch Hand officers (3.6%) than Comparison officers (6.9%) (Table 15-26(b): Adjusted RR=0.46, p=0.047).

There were no significant findings in the unadjusted analyses of Model 3 (Table 15-26(e): p>0.15 for all analyses). In the adjusted analyses of Model 3, a significantly lower percentage of Ranch Hands in the background dioxin category (4.0%) and Ranch Hands in the low dioxin category (3.4%) exhibited abnormal posterior tibial pulses relative to Comparisons (5.9%) (Table 15-27(f): Adjusted RR=0.48, p=0.039 for the background dioxin category contrast; Adjusted RR=0.40, p=0.048 for the low dioxin category contrast).

All unadjusted and adjusted analyses of posterior tibial pulses for Models 2 and 4 were nonsignificant (Table 15-26(c,d,g,h): p>0.07 for all analyses).

Table 15-26. Analysis of Posterior Tibial Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*765*	*33 (4.3)*	*0.72 (0.47,1.10)*	*0.124*
	Comparison	*1,153*	*68 (5.9)*		
Officer	Ranch Hand	302	11 (3.6)	0.51 (0.25,1.04)	0.062
	Comparison	451	31 (6.9)		
Enlisted Flyer	Ranch Hand	129	8 (6.2)	1.03 (0.40,2.65)	0.945
	Comparison	183	11 (6.0)		
Enlisted Groundcrew	Ranch Hand	334	14 (4.2)	0.83 (0.43,1.61)	0.582
	Comparison	519	26 (5.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,860*	*0.59 (0.36,0.95)*	*0.027**
Officer	738	0.46 (0.22,0.99)	0.047*
Enlisted Flyer	298	0.79 (0.26,2.35)	0.668
Enlisted Groundcrew	824	0.66 (0.30,1.42)	0.284

*: Statistically significant (0.010<p-value≤0.050).

Table 15-26. Analysis of Posterior Tibial Pulses (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Abnormal**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	135	4 (3.0)	1.26 (0.90,1.76)	0.179
Medium	142	5 (3.5)		
High	139	9 (6.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
409	1.64 (0.94,2.84)	0.072

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,153	68 (5.9)		
Background RH	348	14 (4.0)	0.66 (0.37,1.20)	0.173
Low RH	205	7 (3.4)	0.57 (0.26,1.25)	0.158
High RH	211	11 (5.2)	0.88 (0.46,1.71)	0.714
Low plus High RH	416	18 (4.3)	0.71 (0.41,1.22)	0.215

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-26. Analysis of Posterior Tibial Pulses (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,126		
Background RH	337	0.48 (0.24,0.96)	0.039*
Low RH	191	0.40 (0.16,0.99)	0.048*
High RH	205	0.99 (0.46,2.12)	0.976
Low plus High RH	396	0.64 (0.34,1.19)	0.155

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.010 < p\text{-value} \le 0.050$).

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\le$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\le$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	11 (4.3)	1.08 (0.87,1.34)	0.482
Medium	252	8 (3.2)		
High	255	13 (5.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\le$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
753	1.13 (0.84,1.52)	0.403

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.8 Leg Pulses

No significant findings were found in the Model 1 through Model 4 unadjusted and adjusted analyses of leg pulses (Table 15-27(a-h): p>0.11 for all analyses).

Table 15-27. Analysis of Leg Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*763*	*66 (8.7)*	*0.86 (0.63,1.18)*	*0.358*
	Comparison	*1,152*	*114 (9.9)*		
Officer	Ranch Hand	300	25 (8.3)	0.67 (0.41,1.10)	0.113
	Comparison	451	54 (12.0)		
Enlisted Flyer	Ranch Hand	129	12 (9.3)	0.84 (0.40,1.79)	0.653
	Comparison	184	20 (10.9)		
Enlisted Groundcrew	Ranch Hand	334	29 (8.7)	1.13 (0.69,1.87)	0.622
	Comparison	517	40 (7.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,856*	*0.82 (0.58,1.17)*	*0.274*
Officer	736	0.65 (0.38,1.11)	0.117
Enlisted Flyer	298	0.78 (0.34,1.82)	0.567
Enlisted Groundcrew	822	1.09 (0.63,1.90)	0.754

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	134	13 (9.7)	1.07 (0.83,1.36)	0.609
Medium	142	9 (6.3)		
High	139	16 (11.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
408	1.19 (0.86,1.64)	0.300

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-27. Analysis of Leg Pulses (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,152	114	(9.9)		
Background RH	347	27	(7.8)	0.79 (0.51,1.23)	0.299
Low RH	204	17	(8.3)	0.82 (0.48,1.40)	0.470
High RH	211	21	(10.0)	0.98 (0.60,1.60)	0.935
Low plus High RH	415	38	(9.2)	0.90 (0.61,1.32)	0.588

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,124		
Background RH	336	0.69 (0.42,1.14)	0.146
Low RH	190	0.67 (0.37,1.23)	0.198
High RH	205	1.24 (0.71,2.16)	0.454
Low plus High RH	395	0.92 (0.60,1.43)	0.719

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	18 (7.0)	1.06 (0.91,1.24)	0.464
Medium	251	24 (9.6)		
High	255	23 (9.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 15-27. Analysis of Leg Pulses (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
751	1.06 (0.87,1.30)	0.561

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.9 Peripheral Pulses

All unadjusted and adjusted analyses for Models 1, 2, and 4 were nonsignificant (Table 15-28(a-d,g,h): p>0.06 for all analyses).

The unadjusted analyses of Model 3 were nonsignificant (Table 15-28(e): p>0.06 for all analyses). When adjusted for covariates, a significantly lower percentage of Ranch Hands in the low dioxin category (10.8%) were found to exhibit abnormal peripheral pulses relative to Comparisons (15.9%) (Table 15-28(f): Adjusted RR=0.61, p=0.046).

Table 15-28. Analysis of Peripheral Pulses

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*761*	*106 (13.9)*	*0.86 (0.66,1.11)*	*0.239*
	Comparison	*1,145*	*182 (15.9)*		
Officer	Ranch Hand	298	43 (14.4)	0.76 (0.51,1.14)	0.190
	Comparison	448	81 (18.1)		
Enlisted Flyer	Ranch Hand	129	15 (11.6)	0.64 (0.33,1.24)	0.188
	Comparison	182	31 (17.0)		
Enlisted Groundcrew	Ranch Hand	334	48 (14.4)	1.07 (0.72,1.59)	0.749
	Comparison	515	70 (13.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,885*	*0.89 (0.68,1.16)*	*0.390*
Officer	743	0.80 (0.53,1.22)	0.300
Enlisted Flyer	304	0.65 (0.33,1.29)	0.220
Enlisted Groundcrew	838	1.11 (0.73,1.67)	0.631

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-28. Analysis of Peripheral Pulses (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	133	16 (12.0)	1.21 (0.99,1.49)	0.065
Medium	142	14 (9.9)		
High	139	26 (18.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
407	1.28 (0.98,1.67)	0.074

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,145	182 (15.9)		
Background RH	346	49 (14.2)	0.90 (0.64,1.27)	0.551
Low RH	203	22 (10.8)	0.64 (0.40,1.02)	0.061
High RH	211	34 (16.1)	0.99 (0.66,1.48)	0.958
Low plus High RH	414	56 (13.5)	0.80 (0.57,1.11)	0.178

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-28. Analysis of Peripheral Pulses (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,135		
Background RH	342	0.91 (0.63,1.30)	0.588
Low RH	199	0.61 (0.37,0.99)	0.046*
High RH	208	1.17 (0.76,1.80)	0.480
Low plus High RH	407	0.85 (0.60,1.20)	0.351

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	255	35 (13.7)	1.06 (0.93,1.21)	0.357
Medium	250	32 (12.8)		
High	255	38 (14.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
749	1.10 (0.93,1.29)	0.265

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.10 Resting Pressure Index (Continuous)

All findings in the Model 1 through Model 4 unadjusted and adjusted analyses of the continuous form of the resting pressure index were nonsignificant (Table 15-29(a-h): p>0.20 for all analyses).

Table 15-29. Analysis of Resting Pressure Index (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*763*	*1.250*	*-0.004 (-0.017,0.010)*	*0.591*
	Comparison	*1,138*	*1.253*		
Officer	Ranch Hand	301	1.266	-0.005 (-0.026,0.017)	0.670
	Comparison	447	1.270		
Enlisted Flyer	Ranch Hand	131	1.226	-0.008 (-0.040,0.025)	0.652
	Comparison	182	1.234		
Enlisted Groundcrew	Ranch Hand	331	1.245	-0.001 (-0.021,0.019)	0.920
	Comparison	509	1.246		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*732*	*1.217*	*0.000 (-0.013,0.013)*	*0.977*
	Comparison	*1,112*	*1.217*		
Officer	Ranch Hand	294	1.230	-0.004 (-0.024,0.016)	0.717
	Comparison	439	1.234		
Enlisted Flyer	Ranch Hand	124	1.214	-0.004 (-0.036,0.027)	0.783
	Comparison	176	1.219		
Enlisted Groundcrew	Ranch Hand	314	1.205	0.006 (-0.014,0.025)	0.575
	Comparison	497	1.200		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	136	1.265	1.265	0.005	-0.003 (0.006)	0.569
Medium	142	1.247	1.247			
High	137	1.239	1.240			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 15-29. Analysis of Resting Pressure Index (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	134	1.234	0.180	-0.007 (0.007)	0.313
Medium	140	1.220			
High	134	1.197			

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,138	1.253	1.254		
Background RH	347	1.250	1.248	-0.005 (-0.023,0.012)	0.567
Low RH	206	1.250	1.251	-0.003 (-0.024,0.019)	0.806
High RH	209	1.250	1.252	-0.002 (-0.023,0.020)	0.885
Low plus High RH	415	1.250	1.251	-0.002 (-0.019,0.014)	0.798

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,112	1.217		
Background RH	336	1.209	-0.008 (-0.025,0.009)	0.358
Low RH	192	1.231	0.014 (-0.007,0.035)	0.203
High RH	203	1.218	0.001 (-0.020,0.023)	0.897
Low plus High RH	395	1.224	0.007 (-0.009,0.023)	0.365

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 15-29. Analysis of Resting Pressure Index (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean**	**R^2**	**Slope (Standard Error)**	**p-Value**
Low	256	1.252	<0.001	-0.001 (0.003)	0.721
Medium	253	1.256			
High	253	1.243			

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	253	1.215	0.136	0.000 (0.004)	0.991
Medium	250	1.228			
High	248	1.220			

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.
Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.11   Resting Pressure Index (Discrete)

All unadjusted and adjusted analyses of the discrete form of resting pressure index in Models 1 through 4 were nonsignificant (Table 15-30(a-h): p>0.06 for all analyses).

Table 15-30. Analysis of Resting Pressure Index (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*763*	*32 (4.2)*	*1.20 (0.75,1.93)*	*0.449*
	Comparison	*1,138*	*40 (3.5)*		
Officer	Ranch Hand	301	13 (4.3)	0.92 (0.45,1.86)	0.807
	Comparison	447	21 (4.7)		
Enlisted Flyer	Ranch Hand	131	8 (6.1)	1.63 (0.57,4.60)	0.360
	Comparison	182	7 (3.8)		
Enlisted Groundcrew	Ranch Hand	331	11 (3.3)	1.42 (0.62,3.27)	0.404
	Comparison	509	12 (2.4)		

Table 15-30. Analysis of Resting Pressure Index (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,844*	*1.00 (0.59,1.71)*	*0.986*
Officer	733	0.83 (0.38,1.79)	0.628
Enlisted Flyer	300	1.30 (0.41,4.11)	0.654
Enlisted Groundcrew	811	1.15 (0.45,2.93)	0.777

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	5 (3.7)	1.05 (0.74,1.48)	0.804
Medium	142	4 (2.8)		
High	137	10 (7.3)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
408	1.37 (0.80,2.32)	0.246

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-30. Analysis of Resting Pressure Index (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,138	40 (3.5)		
Background RH	347	13 (3.7)	1.09 (0.57,2.06)	0.801
Low RH	206	8 (3.9)	1.10 (0.51,2.39)	0.802
High RH	209	11 (5.3)	1.50 (0.75,2.99)	0.247
Low plus High RH	415	19 (4.6)	1.29 (0.73,2.27)	0.378

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,112		
Background RH	336	0.81 (0.39,1.68)	0.565
Low RH	192	0.65 (0.25,1.65)	0.363
High RH	203	2.14 (0.96,4.80)	0.064
Low plus High RH	395	1.20 (0.62,2.32)	0.593

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	10 (3.9)	1.02 (0.82,1.27)	0.882
Medium	253	9 (3.6)		
High	253	13 (5.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 15-30. Analysis of Resting Pressure Index (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
751	0.96 (0.70,1.32)	0.820

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.12 *Hyperemic Pressure Index (1 Minute Post-exercise) (Continuous)*

All Model 1 through Model 4 unadjusted and adjusted analyses of the continuous form of hyperemic pressure index at 1 minute after exercise were nonsignificant (Table 15-31(a-h): p>0.10 for all analyses).

Table 15-31. Analysis of Hyperemic Pressure Index (1 Minute Post-exercise) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*740*	*1.175*	*0.003 (-0.014,0.021)*	*0.697*
	Comparison	*1,108*	*1.172*		
Officer	Ranch Hand	294	1.204	0.001 (-0.026,0.028)	0.923
	Comparison	435	1.202		
Enlisted Flyer	Ranch Hand	123	1.140	0.016 (-0.026,0.058)	0.449
	Comparison	177	1.123		
Enlisted Groundcrew	Ranch Hand	323	1.163	0.001 (-0.025,0.026)	0.964
	Comparison	496	1.163		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*729*	*1.137*	*0.004 (-0.012,0.020)*	*0.628*
	Comparison	*1,100*	*1.133*		
Officer	Ranch Hand	291	1.162	0.004 (-0.021,0.029)	0.739
	Comparison	435	1.157		
Enlisted Flyer	Ranch Hand	120	1.130	0.016 (-0.023,0.056)	0.412
	Comparison	175	1.114		
Enlisted Groundcrew	Ranch Hand	318	1.123	-0.001 (-0.025,0.023)	0.933
	Comparison	490	1.124		

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	130	1.187	1.187	0.003	-0.007 (0.007)	0.349
Medium	136	1.168	1.168			
High	133	1.160	1.161			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	128	1.140	0.190	-0.011 (0.008)	0.179
Medium	134	1.133			
High	130	1.103			

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,108	1.172	1.172		
Background RH	340	1.180	1.177	0.005 (-0.017,0.028)	0.642
Low RH	199	1.178	1.179	0.006 (-0.021,0.034)	0.649
High RH	200	1.166	1.169	-0.004 (-0.031,0.024)	0.803
Low plus High RH	399	1.172	1.174	0.001 (-0.020,0.023)	0.893

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,100	1.131		
Background RH	336	1.127	-0.004 (-0.025,0.017)	0.709
Low RH	195	1.153	0.021 (-0.005,0.047)	0.108
High RH	197	1.135	0.004 (-0.023,0.030)	0.784
Low plus High RH	392	1.144	0.012 (-0.007,0.032)	0.219

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

   Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean	R^2	Slope (Standard Error)	p-Value
Low	252	1.195	0.002	-0.005 (0.004)	0.228
Medium	244	1.166			
High	243	1.165			

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	249	1.127	0.176	-0.001 (0.005)	0.888
Medium	241	1.117			
High	238	1.128			

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.
   Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.13 Hyperemic Pressure Index (1 Minute Post-exercise) (Discrete)

There were no significant findings in the Model 1 through Model 4 unadjusted and adjusted analyses of the discrete form of hyperemic pressure index 1 minute after exercise (Table 15-32(a-h): p>0.24 for all analyses).

Table 15-32. Analysis of Hyperemic Pressure Index (1 Minute Post-exercise) (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low		Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*740*	*72*	*(9.7)*	*1.05 (0.77,1.44)*	*0.755*
	Comparison	*1,108*	*103*	*(9.3)*		
Officer	Ranch Hand	294	21	(7.1)	0.88 (0.50,1.54)	0.653
	Comparison	435	35	(8.0)		
Enlisted Flyer	Ranch Hand	123	22	(17.9)	1.46 (0.77,2.76)	0.245
	Comparison	177	23	(13.0)		
Enlisted Groundcrew	Ranch Hand	323	29	(9.0)	0.99 (0.61,1.61)	0.963
	Comparison	496	45	(9.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,829*	*1.02 (0.72,1.47)*	*0.896*
Officer	726	0.76 (0.40,1.42)	0.383
Enlisted Flyer	295	1.53 (0.74,3.14)	0.252
Enlisted Groundcrew	808	1.04 (0.60,1.79)	0.899

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	130	13 (10.0)	1.03 (0.81,1.32)	0.798
Medium	136	13 (9.6)		
High	133	15 (11.3)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
392	1.12 (0.78,1.59)	0.545

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,108	103 (9.3)		
Background RH	340	31 (9.1)	1.02 (0.67,1.56)	0.925
Low RH	199	20 (10.1)	1.08 (0.65,1.79)	0.760
High RH	200	21 (10.5)	1.10 (0.67,1.81)	0.711
Low plus High RH	399	41 (10.3)	1.09 (0.74,1.60)	0.658

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,100		
Background RH	336	1.05 (0.64,1.71)	0.847
Low RH	195	0.87 (0.49,1.53)	0.622
High RH	197	1.16 (0.66,2.05)	0.610
Low plus High RH	392	1.00 (0.65,1.55)	0.989

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Low**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	252	17 (6.7)	1.09 (0.93,1.26)	0.288
Medium	244	29 (11.9)		
High	243	26 (10.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
728	1.08 (0.87,1.33)	0.488

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.14   Hyperemic Pressure Index (2 Minutes Post-exercise) (Continuous)

No significant findings were found in the Model 1 through Model 4 unadjusted and adjusted analyses of the continuous form of hyperemic pressure index 2 minutes after exercise (Table 15-33(a-h): p>0.14 for all analyses).

Table 15-33. Analysis of Hyperemic Pressure Index (2 Minutes Post-exercise) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*740*	*1.227*	*-0.002 (-0.017,0.014)*	*0.840*
	Comparison	*1,110*	*1.228*		
Officer	Ranch Hand	294	1.250	-0.003 (-0.028,0.021)	0.797
	Comparison	437	1.253		
Enlisted Flyer	Ranch Hand	123	1.200	0.009 (-0.029,0.047)	0.654
	Comparison	177	1.191		
Enlisted Groundcrew	Ranch Hand	323	1.216	-0.004 (-0.027,0.019)	0.742
	Comparison	496	1.220		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*729*	*1.197*	*-0.002 (-0.016,0.013)*	*0.805*
	Comparison	*1,102*	*1.199*		
Officer	Ranch Hand	291	1.221	-0.001 (-0.024,0.022)	0.945
	Comparison	437	1.222		
Enlisted Flyer	Ranch Hand	120	1.196	0.009 (-0.027,0.045)	0.617
	Comparison	175	1.187		
Enlisted Groundcrew	Ranch Hand	318	1.177	-0.007 (-0.028,0.015)	0.541
	Comparison	490	1.184		

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for $\log_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	130	1.237	1.237	0.004	-0.007 (0.006)	0.296
Medium	136	1.221	1.221			
High	133	1.214	1.215			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	128	1.203	0.200	-0.008 (0.007)	0.250
Medium	134	1.200			
High	130	1.178			

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-33. Analysis of Hyperemic Pressure Index (2 Minutes Post-exercise) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,110	1.228	1.229		
Background RH	340	1.230	1.229	0.000 (-0.020,0.021)	0.988
Low RH	199	1.227	1.227	-0.001 (-0.027,0.024)	0.914
High RH	200	1.221	1.223	-0.005 (-0.030,0.020)	0.693
Low plus High RH	399	1.224	1.225	-0.003 (-0.022,0.016)	0.741

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,102	1.198		
Background RH	336	1.189	-0.009 (-0.028,0.011)	0.379
Low RH	195	1.207	0.010 (-0.014,0.033)	0.419
High RH	197	1.198	0.001 (-0.023,0.025)	0.956
Low plus High RH	392	1.203	0.005 (-0.013,0.023)	0.574

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean	R^2	Slope (Standard Error)	p-Value
Low	252	1.240	0.003	-0.005 (0.004)	0.142
Medium	244	1.223			
High	243	1.218			

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	249	1.190	0.184	-0.002 (0.004)	0.579
Medium	241	1.188			
High	238	1.193			

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.3.15 Hyperemic Pressure Index (2 Minutes Post-exercise) (Discrete)

All Model 1 through Model 4 unadjusted and adjusted analyses of the discrete form of hyperemic pressure index 2 minutes after exercise were nonsignificant (Table 15-34(a-h): p≥0.12 for all analyses).

Table 15-34. Analysis of Hyperemic Pressure Index (2 Minutes Post-exercise) (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*740*	*34 (4.6)*	*0.77 (0.51,1.19)*	*0.234*
	Comparison	*1,110*	*65 (5.9)*		
Officer	Ranch Hand	294	11 (3.7)	0.57 (0.28,1.16)	0.120
	Comparison	437	28 (6.4)		
Enlisted Flyer	Ranch Hand	123	8 (6.5)	0.88 (0.35,2.19)	0.779
	Comparison	177	13 (7.3)		
Enlisted Groundcrew	Ranch Hand	323	15 (4.6)	0.96 (0.49,1.85)	0.898
	Comparison	496	24 (4.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,831*	*0.78 (0.48,1.25)*	*0.293*
Officer	728	0.54 (0.25,1.19)	0.129
Enlisted Flyer	295	0.84 (0.31,2.27)	0.735
Enlisted Groundcrew	808	1.05 (0.50,2.22)	0.892

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	130	5 (3.8)	1.10 (0.76,1.57)	0.623
Medium	136	4 (2.9)		
High	133	8 (6.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
392	1.13 (0.62,2.03)	0.696

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,110	65 (5.9)		
Background RH	340	17 (5.0)	0.84 (0.49,1.47)	0.549
Low RH	199	8 (4.0)	0.67 (0.32,1.43)	0.302
High RH	200	9 (4.5)	0.76 (0.37,1.55)	0.450
Low plus High RH	399	17 (4.3)	0.71 (0.41,1.24)	0.230

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,102		
Background RH	336	0.85 (0.45,1.61)	0.625
Low RH	195	0.59 (0.26,1.32)	0.200
High RH	197	0.86 (0.38,1.92)	0.706
Low plus High RH	392	0.71 (0.39,1.30)	0.270

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	252	8 (3.2)	1.05 (0.85,1.30)	0.649
Medium	244	15 (6.1)		
High	243	11 (4.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
728	0.95 (0.70,1.29)	0.757

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.2.2.4   Questionnaire Variable

15.2.2.4.1 Intermittent Claudication and Vascular Insufficiency Index

No significant findings were seen in the Model 1 through Model 4 unadjusted and adjusted analyses of the intermittent claudication and vascular insufficiency index (Table 15-35(a–h): p>0.11 for all analyses).

Table 15-35. Analysis of Intermittent Claudication and Vascular Insufficiency Index

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*767*	*22 (2.9)*	*0.89 (0.52,1.52)*	*0.673*
	Comparison	*1,154*	*37 (3.2)*		
Officer	Ranch Hand	302	8 (2.6)	0.92 (0.38,2.25)	0.857
	Comparison	453	13 (2.9)		
Enlisted Flyer	Ranch Hand	131	4 (3.1)	1.13 (0.30,4.28)	0.860
	Comparison	184	5 (2.7)		
Enlisted Groundcrew	Ranch Hand	334	10 (3.0)	0.81 (0.37,1.76)	0.593
	Comparison	517	19 (3.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,902*	*0.83 (0.47,1.46)*	*0.505*
Officer	752	0.81 (0.31,2.10)	0.662
Enlisted Flyer	308	1.15 (0.29,4.47)	0.844
Enlisted Groundcrew	842	0.75 (0.32,1.71)	0.488

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	2 (1.5)	1.16 (0.77,1.73)	0.490
Medium	142	4 (2.8)		
High	140	6 (4.3)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
411	1.33 (0.77,2.29)	0.308

[a]Relative risk for a twofold increase in initial dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,154	37 (3.2)		
Background RH	348	10 (2.9)	0.98 (0.48,2.00)	0.949
Low RH	206	4 (1.9)	0.58 (0.21,1.65)	0.310
High RH	212	8 (3.8)	1.09 (0.50,2.38)	0.833
Low plus High RH	418	12 (2.9)	0.80 (0.40,1.60)	0.526

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,146		
Background RH	344	0.91 (0.42,1.97)	0.806
Low RH	202	0.38 (0.11,1.27)	0.115
High RH	209	1.19 (0.52,2.74)	0.681
Low plus High RH	411	0.68 (0.31,1.46)	0.320

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

Table 15-35. Analysis of Intermittent Claudication and Vascular Insufficiency Index (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	7 (2.7)	1.09 (0.85,1.42)	0.496
Medium	253	5 (2.0)		
High	256	10 (3.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
755	1.02 (0.72,1.45)	0.899

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Family history of heart disease before the age of 45 was not included in the model (see Section 15.1.4).

15.3 DISCUSSION

Cardiovascular disorders are among the most common diseases encountered by primary care physicians. Although arbitrary, dividing data collection into central and peripheral cardiovascular functions is convenient and forms a reasonable basis for comparing cohorts under study. In practice, diagnosing cardiovascular disease is based primarily on noninvasive data, as analyzed in this chapter. Specifically, history, physical examination, and a resting ECG serve as highly reliable indices that can alert clinicians to the presence of underlying cardiovascular disease and indicate the need for additional, more-specific, noninvasive or invasive studies.

The limitations of the history in diagnosing cardiovascular disease deserve emphasis. For example, in peripheral vascular disease, signs and symptoms will vary depending on the degree of development of collateral circulatory channels. While hemodynamically significant arterial disease of the lower extremities is usually associated with claudication, severe carotid occlusive disease can be present in the absence of symptoms of transient cerebral ischemia. Further, conclusive evidence shows that advanced coronary artery disease can occur in the absence of angina and be present as "silent" myocardial ischemia. Lastly, it is well recognized that cardiovascular history, as related by patients, is often subject to error. The generic term "heart attack," for example, can be used to describe any type of cardiac event ranging from an isolated episode of unstable angina or arrhythmia to a myocardial infarction. These imperfections highlight the importance of medical record verification, as conducted in this study.

In the assessment of the cardiovascular system, the physical examination can provide valuable clues to the presence of asymptomatic but significant underlying disease. In this study, steps were taken to simplify

data collection and reduce interobserver variability among the examining physicians. All blood pressure readings, for example, were taken by automated sphygmomanometric instruments. In the cardiovascular examination, murmurs and bruits were auscultory endpoints generated by turbulent blood flow of valvular or vascular origin, respectively. The detection of subtle variation in the frequency, intensity, and radiation of murmurs enables the experienced cardiologist to predict accurately the specific valve of origin and associated hemodynamic significance. Because these skills are usually not acquired by the general internist, and to minimize interobserver variability, the examination protocol specified the recording of the presence or absence of murmurs and the anatomic location on the chest wall. As markers of occult arterial occlusive disease, vascular bruits were relatively easy to detect and were carefully sought over the carotid, abdominal, and femoral vessels.

Dependent variable-covariate analyses confirmed associations that are well established in clinical practice. When correlated with a medical records review, abnormalities noted during physical examinations and in the laboratory confirmed the association of cardiovascular disease with the classic risk factors of age, cigarette use, family history, diabetes, obesity, and alcohol consumption. In the 1997 examinations, obesity proved to be a significant risk factor for the development of heart disease. In the current study, however, the incidence of heart disease was almost identical in participants who were obese and those who were not obese (82.3% versus 82.2%, respectively), and body mass index was most strongly associated with systolic and diastolic hypertension.

Historically, lifetime alcohol consumption has been strongly associated with hypertension; however, blood pressure determinations made during the 2002 physical examinations did not make this strong association. The increased prevalence of selected pulse deficits associated with alcohol consumption may have been mediated by concomitant cigarette use. Likewise, the finding of significantly lower cholesterol in participants with a history of hypertension, heart disease, and myocardial infarction is counterintuitive, explained perhaps by the use of cholesterol medication by these participants for a heart condition, which was not investigated in these analyses.

In the analyses of verified historical variables, the prevalence of hypertension, myocardial infarction, transient ischemic attack, and stroke was similar in Ranch Hands and Comparisons. At the 1997 examination, in contrast to the 1992 examination, heart disease was more prevalent in Ranch Hands than Comparisons (66.1% versus 60.8%) across all occupational strata. Related to a marked interim increase in heart disease in Comparison relative to Ranch Hand officers, this disparity in prevalence had narrowed (84.0% versus 81.1%) by 2002. The relative risk was statistically significant, though less so, and only in the enlisted flyer category (p=0.004 in 1997 versus p=0.015 in 2002). The Ranch Hand cohort in the 1992 and 1997 examinations showed a significant inverse dose-response effect between heart disease and either initial dioxin or 1987 serum dioxin. In the 2002 follow-up examination, the prevalence of heart disease was not significantly associated with dioxin within the Ranch Hand group.

During the 20-year course of this longitudinal study, the results of the serum dioxin analyses in the cardiovascular assessment have been variable and inconsistent. In the 1997 examinations, significant positive dose-response effects were noted in the associations of hypertension, ECG evidence of prior myocardial infarction, and tachycardia with 1987 serum dioxin levels. In the current study, only diastolic blood pressure (discrete form) was found to have a positive association with dioxin. In a pattern similar to one found in 1997, but in 2002 more pronounced and statistically significant, an increasing dose-response and relative risk was noted in Ranch Hands in the high dioxin category (in 1997: Adjusted RR=1.46, p=0.221; in 2002: Adjusted RR=1.88, p=0.036).

The prevalence of funduscopic abnormalities and intermittent claudication, both more common in Ranch Hands than Comparisons at the 1992 examinations, remained the same in the two cohorts in the current

study as they were in 1997. In several analyses, pulse deficits, also more common in Ranch Hands in 1992 (but not in 1997), were found to be more common in Comparisons in the current study.

At the conclusion of six examinations conducted over 20 years, the prevalence of cardiovascular disease was not significantly increased in the Ranch Hand cohort. In only one analysis, that of diastolic blood pressure noted above, was there any evidence for a dose-response effect in relation to the body burden of dioxin.

15.4   SUMMARY

The cardiovascular assessment was based on questionnaire data, which was subsequently verified by a review of medical records, and physical examination data. Associations with herbicide exposure (i.e., group − Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable in the cardiovascular assessment. The significant adjusted results are discussed in the sections below.

15.4.1   Model 1: Group Analysis

The Model 1 analyses revealed significant findings in the adjusted analyses of heart disease (excluding essential hypertension) and in the adjusted analyses of posterior tibial pulses. The presence of heart disease was found to be significantly higher among Ranch Hands than Comparisons in enlisted flyers. In the adjusted analyses of posterior tibial pulses, Ranch Hands were found to have a significantly lower presence of abnormal pulses than Comparisons. Likewise, in the analysis of officers, a significantly greater percentage of Comparisons were found to have abnormal posterior tibial pulses than Ranch Hands. The results of the group analysis are provided in Table 15-36.

Table 15-36. Summary of Group Analysis (Model 1) for Cardiovascular Variables (Ranch Hands vs. Comparisons)

Dependent Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records Data				
Essential Hypertension (D)	ns	ns	ns	NS
Heart Disease (excluding Essential Hypertension) (D)	NS	ns	p=0.010 (2.56)	NS
Myocardial Infarction (D)	ns	ns	ns	NS
Stroke or Transient Ischemic Attack (D)	NS	NS	NS	NS
Physical Examination				
Systolic Blood Pressure (C)	ns	ns	ns	p=0.045 (-2.4)
Systolic Blood Pressure (D)	ns	ns	ns	ns
Diastolic Blood Pressure (C)	ns	ns	ns	ns
Diastolic Blood Pressure (D)	NS	ns	ns	NS
Heart Sounds (D)	NS	ns	NS	NS
Overall ECG (D)	NS	ns	NS	ns
ECG: RBBB (D)	NS	NS	NS	ns
ECG: LBBB (D)	ns	ns	NS	NS
ECG: Nonspecific ST- and T-wave Changes (D)	NS	ns	NS	ns
ECG: Bradycardia (D)	NS	NS	NS	ns
ECG: Tachycardia (D)	ns	ns	ns	ns

Table 15-36. Summary of Group Analysis (Model 1) for Cardiovascular Variables (Ranch Hands vs. Comparisons) (Continued)

Dependent Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
ECG: Arrhythmia (D)	ns	ns	ns	ns
ECG: Evidence of Prior Myocardial Infarction (D)	ns	NS	ns	ns
Funduscopic Examination (D)	NS	NS	NS	NS
Carotid Bruits (D)	ns	ns	NS	NS
Radial Pulses (D)	ns	NS	ns	ns
Femoral Pulses (D)	NS	NS	NS	NS
Popliteal Pulses (D)	ns	ns	NS	NS
Dorsalis Pedis Pulses (D)	ns	ns	ns	NS
Posterior Tibial Pulses (D)	ns	ns	NS	ns
Leg Pulses (D)	ns	ns	ns	NS
Peripheral Pulses (D)	ns	ns	ns	NS
Resting Pressure Index (C)[a]	ns	ns	ns	ns
Resting Pressure Index (D)	NS	ns	NS	NS
Hyperemic Pressure Index (1 minute post-exercise) (C)[a]	NS	NS	NS	NS
Hyperemic Pressure Index (1 minute post-exercise) (D)	NS	ns	NS	ns
Hyperemic Pressure Index (2 minutes post-exercise) (C)[a]	ns	ns	NS	ns
Hyperemic Pressure Index (2 minutes post-exercise) (D)	ns	ns	ns	ns
Intermittent Claudication and Vascular Insufficiency Index (D)	ns	ns	NS	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: NS or ns: Not significant (p>0.05).
       C: Continuous form of dependent variable.
       D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

Dependent Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records Data				
Essential Hypertension (D)	ns	ns	ns	NS
Heart Disease (excluding Essential Hypertension) (D)	NS	ns	p=0.015 (2.46)	NS
Myocardial Infarction (D)	ns	ns	ns	NS
Stroke or Transient Ischemic Attack (D)	NS	NS	NS	NS

Dependent Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Physical Examination				
Systolic Blood Pressure (C)	ns	ns	ns	ns
Systolic Blood Pressure (D)	ns	ns	ns	ns
Diastolic Blood Pressure (C)	ns	NS	ns	ns
Diastolic Blood Pressure (D)	NS	ns	NS	NS
Heart Sounds (D)	NS	ns	NS	NS
Overall ECG (D)	NS	ns	NS	ns
ECG: RBBB (D)	NS	NS	ns	ns
ECG: LBBB (D)	ns	ns	--	ns
ECG: Nonspecific ST- and T-wave Changes (D)	NS	ns	NS	ns
ECG: Bradycardia (D)	NS	NS	NS	NS
ECG: Tachycardia (D)	ns	--	--	ns
ECG: Arrhythmia (D)	ns	ns	ns	ns
ECG: Evidence of Prior Myocardial Infarction (D)	ns	NS	ns	ns
Funduscopic Examination (D)	NS	NS	NS	NS
Carotid Bruits (D)	ns	ns	NS	NS
Radial Pulses (D)	ns	NS	ns	ns
Femoral Pulses (D)	NS	NS	NS	NS
Popliteal Pulses (D)	ns	ns	NS	ns
Dorsalis Pedis Pulses (D)	ns	ns	ns	NS
Posterior Tibial Pulses (D)	p=0.027 (0.59)	p=0.047 (0.46)	ns	ns
Leg Pulses (D)	ns	ns	ns	NS
Peripheral Pulses (D)	ns	ns	ns	NS
Resting Pressure Index (C)[a]	NS	ns	ns	NS
Resting Pressure Index (D)	NS	ns	NS	NS
Hyperemic Pressure Index (1 minute post-exercise) (C)[a]	NS	NS	NS	ns
Hyperemic Pressure Index (1 minute post-exercise) (D)	NS	ns	NS	NS
Hyperemic Pressure Index (2 minutes post-exercise) (C)[a]	ns	ns	NS	ns
Hyperemic Pressure Index (2 minutes post-exercise) (D)	ns	ns	ns	NS
Intermittent Claudication and Vascular Insufficiency Index (D)	ns	ns	NS	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
  C: Continuous form of dependent variable.
  D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

15.4.2   Model 2: Initial Dioxin Analysis

There were no significant findings in the adjusted analyses of Model 2. The results of the initial dioxin analysis are shown in Table 15-37.

Table 15-37. Summary of Initial Dioxin Analysis (Model 2) for Cardiovascular Variables (Ranch Hands Only)

Dependent Variable	Unadjusted	Adjusted
Medical Records Data		
Essential Hypertension (D)	NS	NS
Heart Disease (excluding Essential Hypertension) (D)	ns	NS
Myocardial Infarction (D)	NS	NS
Stroke or Transient Ischemic Attack (D)	NS	NS
Physical Examination		
Systolic Blood Pressure (C)	NS	NS
Systolic Blood Pressure (D)	ns	ns
Diastolic Blood Pressure (C)	NS	ns
Diastolic Blood Pressure (D)	NS	NS
Heart Sounds (D)	NS	ns
Overall ECG (D)	ns	NS
ECG: RBBB (D)	NS	NS
ECG: LBBB (D)	NS	NS
ECG: Nonspecific ST- and T-wave Changes (D)	ns	NS
ECG: Bradycardia (D)	ns	NS
ECG: Tachycardia (D)	NS	NS
ECG: Arrhythmia (D)	p=0.001 (0.63)	ns
ECG: Evidence of Prior Myocardial Infarction (D)	NS	NS
Funduscopic Examination (D)	NS	NS
Carotid Bruits (D)	NS	NS
Radial Pulses (D)	NS	NS
Femoral Pulses (D)	ns	ns
Popliteal Pulses (D)	ns	ns
Dorsalis Pedis Pulses (D)	NS	NS
Posterior Tibial Pulses (D)	NS	NS
Leg Pulses (D)	NS	NS

Dependent Variable	Unadjusted	Adjusted
Peripheral Pulses (D)	NS	NS
Resting Pressure Index (C)[a]	ns	ns
Resting Pressure Index (D)	NS	NS
Hyperemic Pressure Index (1 minute post-exercise) (C)[a]	ns	ns
Hyperemic Pressure Index (1 minute post-exercise) (D)	NS	NS
Hyperemic Pressure Index (2 minutes post-exercise) (C)[a]	ns	ns
Hyperemic Pressure Index (2 minutes post-exercise) (D)	NS	NS
Intermittent Claudication and Vascular Insufficiency Index (D)	NS	NS

[a]A negative slope was considered adverse for this variable.

Note: NS or ns: Not significant (p>0.05).
　　　C: Continuous form of dependent variable.
　　　D: Discrete form of dependent variable.

　　　The p-value was given if $p \leq 0.05$. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

　　　A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

15.4.3   Model 3: Categorized Dioxin Analysis

Results for the Model 3 adjusted analyses revealed significant findings in both the continuous and discrete forms of systolic blood pressure. In the analyses of the continuous form, Ranch Hands in both the low dioxin category and the low and high dioxin categories combined were found to have a significantly lower mean systolic blood pressure than Comparisons. Similarly, in the analyses of the discrete form of systolic blood pressure, there was a significantly greater percentage of Comparisons with high systolic blood pressure as compared to Ranch Hands in both the low dioxin category and the low and high dioxin categories combined. In the adjusted analyses of the discrete form of diastolic blood pressure, a significantly greater percentage of Ranch Hands in the high dioxin category were found to have high diastolic blood pressure than Comparisons.

Adjusted Model 3 analyses also revealed significant findings for posterior tibial pulses and peripheral pulses. Abnormal posterior tibial pulses were found among a significantly higher percentage of Comparisons than Ranch Hands in both the background dioxin category and the low dioxin category. In addition, abnormal peripheral pulses were found among a significantly higher percentage of Comparisons than Ranch Hands in the low dioxin category.

The results of the categorized dioxin analysis are presented in Table 15-38.

Table 15-38. Summary of Categorized Dioxin Analysis (Model 3) for Cardiovascular Variables (Ranch Hands vs. Comparisons)

Dependent Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records Data				
Essential Hypertension (D)	ns	ns	NS	NS
Heart Disease (excluding Essential Hypertension) (D)	p=0.019 (1.50)	NS	ns	NS
Myocardial Infarction (D)	ns	ns	ns	ns
Stroke or Transient Ischemic Attack (D)	NS	NS	NS	NS
Physical Examination				
Systolic Blood Pressure (C)	ns	ns	ns	p=0.015 (-2.3)
Systolic Blood Pressure (D)	NS	p=0.035 (0.67)	ns	p=0.010 (0.70)
Diastolic Blood Pressure (C)	ns	ns	NS	NS
Diastolic Blood Pressure (D)	ns	ns	p=0.019 (1.92)	NS
Heart Sounds (D)	NS	NS	NS	NS
Overall ECG (D)	NS	NS	ns	ns
ECG: RBBB (D)	NS	ns	NS	ns
ECG: LBBB (D)	NS	ns	ns	ns
ECG: Nonspecific ST- and T-wave Changes (D)	NS	ns	NS	ns
ECG: Bradycardia (D)	p=0.034 (1.69)	NS	ns	ns
ECG: Tachycardia (D)	ns	ns	ns	ns
ECG: Arrhythmia (D)	ns	NS	p=0.019 (0.49)	ns
ECG: Evidence of Prior Myocardial Infarction (D)	ns	ns	ns	ns
Funduscopic Examination (D)	NS	NS	NS	NS
Carotid Bruits (D)	NS	ns	ns	ns
Radial Pulses (D)	NS	ns	ns	ns
Femoral Pulses (D)	NS	p=0.041 (3.15)	NS	NS
Popliteal Pulses (D)	ns	NS	ns	ns
Dorsalis Pedis Pulses (D)	ns	ns	NS	ns
Posterior Tibial Pulses (D)	ns	ns	ns	ns
Leg Pulses (D)	ns	ns	ns	ns
Peripheral Pulses (D)	ns	ns	ns	ns
Resting Pressure Index (C)[a]	ns	ns	ns	ns
Resting Pressure Index (D)	NS	NS	NS	NS
Hyperemic Pressure Index (1 minute post-exercise) (C)[a]	NS	NS	ns	NS
Hyperemic Pressure Index (1 minute post-exercise) (D)	NS	NS	NS	NS
Hyperemic Pressure Index (2 minutes post-exercise) (C)[a]	NS	ns	ns	ns
Hyperemic Pressure Index (2 minutes post-exercise) (D)	ns	ns	ns	ns
Intermittent Claudication and Vascular Insufficiency Index (D)	ns	ns	NS	ns

Table 15-38. Summary of Categorized Dioxin Analysis (Model 3) for Cardiovascular Variables (Ranch Hands vs. Comparisons) (Continued)

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: NS or ns: Not significant (p>0.05).
   C: Continuous form of dependent variable.
   D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

Dependent Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records Data				
Essential Hypertension (D)	ns	ns	NS	NS
Heart Disease (excluding Essential Hypertension) (D)	NS	NS	NS	NS
Myocardial Infarction (D)	ns	ns	NS	ns
Stroke or Transient Ischemic Attack (D)	NS	NS	NS	NS
Physical Examination				
Systolic Blood Pressure (C)	NS	p=0.025 (-2.9)	ns	p=0.022 (-2.3)
Systolic Blood Pressure (D)	NS	p=0.018 (0.63)	ns	p=0.023 (0.72)
Diastolic Blood Pressure (C)	ns	ns	ns	ns
Diastolic Blood Pressure (D)	ns	ns	p=0.036 (1.88)	NS
Heart Sounds (D)	NS	NS	NS	NS
Overall ECG (D)	NS	ns	ns	ns
ECG: RBBB (D)	NS	ns	NS	ns
ECG: LBBB (D)	ns	ns	ns	ns
ECG: Nonspecific ST- and T-wave Changes (D)	NS	ns	NS	ns
ECG: Bradycardia (D)	NS	NS	ns	NS
ECG: Tachycardia (D)	NS	--	ns	--
ECG: Arrhythmia (D)	ns	NS	ns	ns
ECG: Evidence of Prior Myocardial Infarction (D)	ns	ns	ns	ns
Funduscopic Examination (D)	NS	NS	NS	NS
Carotid Bruits (D)	ns	ns	ns	ns
Radial Pulses (D)	NS	ns	ns	ns
Femoral Pulses (D)	ns	NS	NS	NS
Popliteal Pulses (D)	ns	ns	NS	ns
Dorsalis Pedis Pulses (D)	ns	ns	NS	NS
Posterior Tibial Pulses (D)	p=0.039 (0.48)	p=0.048 (0.40)	ns	ns
Leg Pulses (D)	ns	ns	NS	ns

	ADJUSTED			
Dependent Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Peripheral Pulses (D)	ns	p=0.046 (0.61)	NS	ns
Resting Pressure Index (C)[a]	ns	NS	NS	NS
Resting Pressure Index (D)	ns	ns	NS	NS
Hyperemic Pressure Index (1 minute post-exercise) (C)[a]	ns	NS	NS	NS
Hyperemic Pressure Index (1 minute post-exercise) (D)	NS	ns	NS	NS
Hyperemic Pressure Index (2 minutes post-exercise) (C)[a]	ns	NS	NS	NS
Hyperemic Pressure Index (2 minutes post-exercise) (D)	ns	ns	ns	ns
Intermittent Claudication and Vascular Insufficiency Index (D)	ns	ns	NS	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
   C: Continuous form of dependent variable.
   D: Discrete form of dependent variable.

   The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

   A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

15.4.4 Model 4: 1987 Dioxin Level Analysis

In the Model 4 adjusted analysis of the discrete form of systolic blood pressure, a significant relation was found between presence of high systolic blood pressure and the 1987 dioxin level. As the 1987 dioxin level increased, the percentage of participants with high systolic blood pressure decreased. The results of the 1987 dioxin analysis are displayed in Table 15-39.

Table 15-39. Summary of 1987 Dioxin Analysis (Model 4) for Cardiovascular Variables (Ranch Hands Only)

Dependent Variable	Unadjusted	Adjusted
Medical Records Data		
Essential Hypertension (D)	p<0.001 (1.18)	NS
Heart Disease (excluding Essential Hypertension) (D)	ns	ns
Myocardial Infarction (D)	NS	NS
Stroke or Transient Ischemic Attack (D)	NS	NS
Physical Examination		
Systolic Blood Pressure (C)	ns	ns
Systolic Blood Pressure (D)	ns	p=0.023 (0.86)
Diastolic Blood Pressure (C)	NS	ns
Diastolic Blood Pressure (D)	NS	NS
Heart Sounds (D)	NS	NS
Overall ECG (D)	ns	ns
ECG: RBBB (D)	ns	ns
ECG: LBBB (D)	ns	ns
ECG: Nonspecific ST- and T-wave Changes (D)	NS	ns
ECG: Bradycardia (D)	p=0.024 (0.80)	ns
ECG: Tachycardia (D)	NS	ns
ECG: Arrhythmia (D)	ns	ns
ECG: Evidence of Prior Myocardial Infarction (D)	ns	NS
Funduscopic Examination (D)	NS	NS
Carotid Bruits (D)	ns	ns
Radial Pulses (D)	NS	NS
Femoral Pulses (D)	ns	ns
Popliteal Pulses (D)	NS	ns
Dorsalis Pedis Pulses (D)	NS	NS
Posterior Tibial Pulses (D)	NS	NS
Leg Pulses (D)	NS	NS
Peripheral Pulses (D)	NS	NS
Resting Pressure Index (C)[a]	ns	NS
Resting Pressure Index (D)	NS	ns
Hyperemic Pressure Index (1 minute post-exercise) (C)[a]	ns	ns
Hyperemic Pressure Index (1 minute post-exercise) (D)	NS	NS
Hyperemic Pressure Index (2 minutes post-exercise) (C)[a]	ns	ns
Hyperemic Pressure Index (2 minutes post-exercise) (D)	NS	ns
Intermittent Claudication and Vascular Insufficiency Index (D)	NS	NS

[a]A negative slope was considered adverse for this variable.

Note: NS or ns: Not significant (p>0.05).
         C: Continuous form of dependent variable.
         D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

15.4.5 Summary of Significant Results

Table 15-40 summarizes the significant results (p≤0.05) for the adjusted analyses that were performed for the cardiovascular assessment. The dependent variable and its table reference are listed along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and is explained in footnotes.

Table 15-40. Summary of Results from Significant Adjusted Analyses in the Cardiovascular Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Heart Disease (Excluding Essential Hypertension) (15-4)	1	RH vs. C, Enlisted Flyer	0.015	2.46 (1.19,5.11)	RH: 91.6% C: 81.0%	(a)
Systolic Blood Pressure (Continuous) (15-7)	3	Low RH vs. C	0.025	-2.9	RH: 127.6 mm Hg C: 130.5 mm Hg	(b)
	3	Low plus High RH vs. C	0.022	-2.3	RH: 128.2 mm Hg C: 130.5 mm Hg	(b)
Systolic Blood Pressure (Discrete) (15-8)	3	Low RH vs. C	0.018	0.63 (0.43,0.92)	RH: 19.4% C: 26.0%	(c)
	3	Low plus High RH vs. C	0.023	0.72 (0.54,0.96)	RH: 20.3% C: 26.0%	(c)
	4	All RH: 1987 Dioxin	0.023	0.86 (0.75,0.98)	Low: 26.2% Medium: 21.7% High: 20.7%	(d)
Diastolic Blood Pressure (Discrete) (15-10)	3	High RH vs. C	0.036	1.88 (1.04,3.39)	RH: 9.0% C: 4.8%	(c)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Posterior Tibial Pulses (15-26)	1	RH vs. C, All	0.027	0.59 (0.36,0.95)	RH: 4.3% C: 5.9%	(a)
	1	RH vs. C, Officer	0.047	0.46 (0.22,0.99)	RH: 3.6% C: 6.9%	(a)
	3	Background RH vs. C	0.039	0.48 (0.24,0.96)	RH: 4.0% C: 5.9%	(c)
	3	Low RH vs. C	0.048	0.40 (0.16,0.99)	RH: 3.4% C: 5.9%	(c)
Peripheral Pulses (15-28)	3	Low RH vs. C	0.046	0.61 (0.37,0.99)	RH: 10.8% C: 15.9%	(c)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(b): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each dioxin category in contrast.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

Note: RH = Ranch Hand.
          C = Comparison.

          Model 3: Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
                    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
                    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

          Model 4: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

15.5 CONCLUSION

The presence of heart disease was found to be higher among Ranch Hands than Comparisons in enlisted flyers. Ranch Hands were found to have a lower presence of abnormal pulses, both in all participants and in the officer stratum. No significant relations between cardiovascular endpoints and initial dioxin were observed.

An increased percentage of Ranch Hands in the high dioxin category were found to have abnormally high diastolic blood pressure. Ranch Hands in both the low dioxin category and the low and high dioxin categories combined were found to have a lower mean systolic blood pressure. Similarly, a smaller percentage of Ranch Hands in both the low dioxin category and the low and high dioxin categories combined had an abnormally high systolic blood pressure.

A lower percentage of Ranch Hands in both the background dioxin category and the low dioxin category had abnormal posterior tibial pulses. In addition, abnormal peripheral pulses were found among a lower

percentage of Ranch Hands in the low dioxin category. As the 1987 dioxin level increased, the percentage of participants with abnormally high systolic blood pressure decreased.

The prevalence of cardiovascular disease was not increased in the Ranch Hand cohort. In only one analysis, that of diastolic blood pressure noted above, was there any evidence for a dose-response effect in relation to the body burden of dioxin.

REFERENCES

1. Beaglehole, R., and P. Magnus. 2002. The search for new risk factors for coronary heart disease: Occupational therapy for epidemiologists? *International Journal of Epidemiology* 31:1117-22.

2. Rashid, M.N., F. Fuentes, R.C. Touchon, and P.S. Wehner. 2003. Obesity and the risk for cardiovascular disease. *Preventive Cardiology* 6:42-7.

3. Hu, F.B. 2002. The impact of diabetes and prediabetes on risk of cardiovascular disease and mortality. *Drugs Today (Barc)* 38:769-75.

4. Riecke, K., D. Grimm, M. Shakibaei, P. Kossmehl, G. Schulze-Tanzil, M. Paul, and R. Stahlmann. 2002. Low doses of 2,3,7,8-tetrachlorodibenzo-p-dioxin increase transforming growth factor beta and cause myocardial fibrosis in marmosets (*Callithrix jacchus*). *Archives of Toxicology* 76:360-6.

5. Hermansky, S.J., T.L. Holcslaw, W.J. Murray, R.S. Markin, and S.J. Stohs. 1988. Biochemical and functional effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on the heart of female rats. *Toxicology and Applied Pharmacology* 95:175-84.

6. Canga, L., R. Levi, and A.B. Rifkind. 1988. Heart as a target organ in 2,3,7,8-tetrachlorodibenzo-p-dioxin toxicity: Decreased beta-adrenergic responsiveness and evidence of increased intracellular calcium. *Proceedings of the National Academy of Sciences of the United States of America* 85:905-9.

7. Kociba, R.J., D.G. Keyes, J.E. Beyer, R.M. Carreon, C.E. Wade, D.A. Dittenber, R.P. Kalnins, L.E. Frauson, C.N. Park, S.D. Barnard, R.A. Hummel, and C.G. Humiston. 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. *Toxicology and Applied Pharmacology* 46:279-303.

8. Kelling, C.K., L.A. Menahan, and R.E. Peterson. 1987. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin treatment on mechanical function of the rat heart. *Toxicology and Applied Pharmacology* 91:497-501.

9. Brewster, D.W., F. Matsumura, and T. Akera. 1987. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on guinea pig heart muscle. *Toxicology and Applied Pharmacology* 89:408-17.

10. Walker, M.K., and T.F. Catron. 2000. Characterization of cardiotoxicity induced by 2,3,7,8-tetrachlorodibenzo-p-dioxin and related chemicals during early chick embryo development. *Toxicology and Applied Pharmacology* 167:210-21.

11. Heid, S.E., M.K. Walker, and H.I. Swanson. 2001. Correlation of cardiotoxicity mediated by halogenated aromatic hydrocarbons to aryl hydrocarbon receptor activation. *Toxicological Sciences* 61:187-96.

12. Brewster, D.W., D.W. Bombick, and F. Matsumura. 1988. Rabbit serum hypertriglyceridemia after administration of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Journal of Toxicology and Environmental Health* 25:495-507.

13. Brewster, D.W., and F. Matsumura. 1989. Differential effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin on adipose tissue lipoprotein lipase activity in the guinea pig, rat, hamster, rabbit, and mink. *Comparative Biochemistry and Physiology – Part C: Toxicology and Pharmacology* 93:49-53.

14. Cantrell, S.M., L.H. Lutz, D.E. Tillitt, and M. Hannink. 1996. Embryotoxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD): The embryonic vasculature is a physiological target for TCDD-induced DNA damage and apoptotic cell death in Medaka (*Orizias latipes*). *Toxicology and Applied Pharmacology* 141:23-34.

15. Guiney, P.D., R.M. Smolowitz, R.E. Peterson, and J.J. Stegeman. 1997. Correlation of 2,3,7,8-tetrachlorodibenzo-p-dioxin induction of cytochrome P4501A in vascular endothelium with toxicity in early life stages of lake trout. *Toxicology and Applied Pharmacology* 143:256-73.

16. Anonymous. 1980. No excess in cancer deaths found in largest group ever studied for long-term effects of dioxin exposure. *American Industrial Hygiene Association Journal* 41:73.

17. Assennato, G., D. Cervino, E.A. Emmett, G. Longo, and F. Merlo. 1989. Follow-up of subjects who developed chloracne following TCDD exposure at Seveso. *American Journal of Industrial Medicine* 16:119-25.

18. Bertazzi, P.A., I. Bernucci, G. Brambilla, D. Consonni, and A.C. Pesatori. 1998. The Seveso studies on early and long-term effects of dioxin exposure: A review. *Environmental Health Perspectives* 106(Suppl 2):625-33.

19. Bertazzi, P.A. 1991. Long-term effects of chemical disasters. Lessons and results from Seveso. *The Science of the Total Environment* 106:5-20.

20. Bertazzi, P.A., C. Zocchetti, A.C. Pesatori, S. Guercilena, M. Sanarico, and L. Radice. 1989. Ten-year mortality study of the population involved in the Seveso incident in 1976. *American Journal of Epidemiology* 129:1187-200.

21. Bertazzi, P.A., C. Zocchetti, A.C. Pesatori, S. Guercilena, M. Sanarico, and L. Radice. 1989. Mortality in an area contaminated by TCDD following an industrial incident. *La Medicina del Lavoro* 80:316-29.

22. Bertazzi, P.A., D. Consonni, S. Bachetti, M. Rubagotti, A. Baccarelli, C. Zocchetti, and A.C. Pesatori. 2001. Health effects of dioxin exposure: A 20-year mortality study. *American Journal of Epidemiology* 153:1031-44.

23. Hoffman, R.E., P.A. Stehr-Green, K.B. Webb, R.G. Evans, A.P. Knutsen, W.F. Schramm, J.L. Staake, B.B. Gibson, and K.K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *The Journal of the American Medical Association* 255:2031-8.

24. Pesatori, A.C., C. Zocchetti, S. Guercilena, D. Consonni, D. Turrini, and P.A. Bertazzi. 1998. Dioxin exposure and non-malignant health effects: A mortality study. *Occupational and Environmental Medicine* 55:126-31.

25. Revich, B., E. Aksel, T. Ushakova, I. Ivanova, N. Zhuchenko, N. Klyuev, B. Brodsky, and Y. Sotskov. 2001. Dioxin exposure and public health in Chapaevsk, Russia. *Chemosphere* 43:951-66.

26. Signorini, S., P.M. Gerthoux, C. Dassi, M. Cazzaniga, P. Brambilla, N. Vincoli, and P. Mocarelli. 2000. Environmental exposure to dioxin: The Seveso experience. *Andrologia* 32:263-70.

27. Stehr, P.A., G. Stein, K. Webb, W. Schramm, W.B. Gedney, H.D. Donnell, S. Ayres, H. Falk, E. Sampson, S.J. Smith, and K. Steinberg. 1986. A pilot epidemiologic study of possible health effects associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin contaminations in Missouri. *Archives of Environmental Health* 41:16-22.

28. Pesatori, A.C., D. Consonni, S. Bachetti, C. Zocchetti, M. Bonzini, A. Baccarelli, and P.A. Bertazzi. 2003. Short- and long-term morbidity and mortality in the population exposed to dioxin after the "Seveso Accident." *Industrial Health* 41:127-38.

29. Becher, H., D. Flesch-Janys, T. Kauppinen, M. Kogevinas, K. Steindorf, A. Manz, and J. Wahrendorf. 1996. Cancer mortality in German male workers exposed to phenoxy herbicides and dioxins. *Cancer Causes Control* 7:312-21.

30. Bond, G.G., M.G. Ott, F.E. Brenner, and R.R. Cook. 1983. Medical and morbidity surveillance findings among employees potentially exposed to TCDD. *British Journal of Industrial Medicine* 40:318-24.

31. Burns, C.J., K.K. Beard, and J.B. Cartmill. 2001. Mortality in chemical workers potentially exposed to 2,4-dichlorophenoxyacetic acid (2,4-D) 1945-94: An update. *Occupational and Environmental Medicine* 58: 24-30.

32. Calvert, G.M., D.K. Wall, M.H. Sweeney, and M.A. Fingerhut. 1998. Evaluation of cardiovascular outcomes among U.S. workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Environmental Health Perspectives* 106(Suppl 2):635-43.

33. Coggon, D., B. Pannett, and P. Winter. 1991. Mortality and incidence of cancer at four factories making phenoxy herbicides. *British Journal of Industrial Medicine* 48:173-8.

34. Collins, J.J., M.E. Strauss, G.J. Levinskas, and P.R. Conner. 1993. The mortality experience of workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin in a trichlorophenol process accident. *Epidemiology* 4:7-13.

35. Cook, R.R., G.G. Bond, R.A. Olson, and M.G. Ott. 1987. Update of the mortality experience of workers exposed to chlorinated dioxins. *Chemosphere* 16:2111-6.

36. Cook, R.R., G.G. Bond, R.A. Olson, M.G. Ott, and M.R. Gondek. 1986. Evaluation of the mortality experience of workers exposed to the chlorinated dioxins. *Chemosphere* 15:1769-76.

37. Flesch-Janys, D. 1997. Analyses of exposure to polychlorinated dibenzo-p-dioxins, furans, and hexachlorocyclohexane and different health outcomes in a cohort of former herbicide-producing workers in Hamburg, Germany. *Teratogenesis, Carcinogenesis and Mutagenesis* 17:257-64.

38. Flesch-Janys, D., J. Berger, P. Gurn, A. Manz, S. Nagel, H. Waltsgott, and J.H. Dwyer. 1995. Exposure to polychlorinated dioxins and furans (PCDD/F) and mortality in a cohort of workers from a herbicide-producing plant in Hamburg, Federal Republic of Germany. *American Journal of Epidemiology* 142:1165-75.

39. Hooiveld, M., D.J. Heederik, M. Kogevinas, P. Boffetta, L.L. Needham, D.G. Patterson, Jr., and H.B. Bueno-de-Mesquita. 1998. Second follow-up of a Dutch cohort occupationally exposed to phenoxy herbicides, chlorophenols, and contaminants. *American Journal of Epidemiology* 147:891-901.

40. Kitamura, K., Y. Kikuchi, S. Watanabe, G. Waechter, H. Sakurai, and T. Takada. 2000. Health effects of chronic exposure to polychlorinated dibenzo-P-dioxins (PCDD), dibenzofurans (PCDF) and coplanar PCB (Co-PCB) of municipal waste incinerator workers. *Journal of Epidemiology/Japan Epidemiological Association* 10:262-70.

41. Kogevinas, M., H. Becher, T. Benn, P.A. Bertazzi, P. Boffetta, H.B. Bueno-de-Mesquita, D. Coggon, D. Colin, D. Flesch-Janys, M. Fingerhut, L. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, N. Pearce, and R. Saracci. 1997. Cancer mortality in workers exposed to phenoxy herbicides, chlorophenols, and dioxins. An expanded and updated international cohort study. *American Journal of Epidemiology* 145:1061-75.

42. Moses, M., R. Lilis, K.D. Crow, J. Thornton, A. Fischbein, H.A. Anderson, and I.J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *American Journal of Industrial Medicine* 5:161-82.

43. Ott, M.G., R.A. Olson, R.R. Cook, and G.G. Bond. 1987. Cohort mortality study of chemical workers with potential exposure to the higher chlorinated dioxins. *Journal of Occupational Medicine* 29:422-9.

44. Ott, M.G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.

45. Ott, M.G., B.B. Holder, and R.D. Olson. 1980. A mortality analysis of employees engaged in the manufacture of 2,4,5-trichlorophenoxyacetic acid. *Journal of Occupational Medicine* 22:47-50.

46. Ott, M.G., and A. Zober. 1996. Cause specific mortality and cancer incidence among employees exposed to 2,3,7,8-TCDD after a 1953 reactor accident. *Occupational and Environmental Medicine* 53:606-12.

47. Ramlow, J.M., N.W. Spadacene, S.R. Hoag, B.A. Stafford, J.B. Cartmill, and P.J. Lerner. 1996. Mortality in a cohort of pentachlorophenol manufacturing workers, 1940-1989. *American Journal of Industrial Medicine* 30:180-94.

48. Steenland, K., L. Piacitelli, J. Deddens, M. Fingerhut, and L.I. Chang. 1999. Cancer, heart disease, and diabetes in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of the National Cancer Institute* 91:779-86.

49. Suskind, R.R., and V.S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *The Journal of the American Medical Association* 251:2372-80.

50. Thiess, A.M., R. Frentzel-Beyme, and R. Link. 1982. Mortality study of persons exposed to dioxin in a trichlorophenol-process accident that occurred in the BASF AG on November 17, 1953. *American Journal of Industrial Medicine* 3:179-89.

51. Thomas, T.L. 1987. Mortality among flavour and fragrance chemical plant workers in the United States. *British Journal of Industrial Medicine* 44:733-7.

52. Vena, J., P. Boffetta, H. Becher, T. Benn, H.B. Bueno-de-Mesquita, D. Coggon, D. Colin, D. Flesch-Janys, L. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, N. Pearce, A.C. Pesatori, R. Saracci, K. Steenland, and M. Kogevinas. 1998. Exposure to dioxin and nonneoplastic mortality in the expanded IARC international cohort study of phenoxy herbicide and chlorophenol production workers and sprayers. *Environmental Health Perspectives* 106(Suppl 2):645-53.

53. Von Benner, A., L. Edler, K. Mayer, and A. Zober. 1994. 'Dioxin' investigation program of the chemical industry professional association. *Arbeitsmedizin Sozialmedizin Praventivmedizin* 29:11-6.

54. Zack, J.A., and W.R. Gaffey. 1983. A mortality study of workers employed at the Monsanto company plant in Nitro, West Virginia. *Environmental Science Research* 26:575-91.

55. Zack, J.A., and R.R. Suskind. 1980. The mortality experience of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident. *Journal of Occupational Medicine* 22:11-4.

56. Zober, A., M.G. Ott, and P. Messerer. 1994. Morbidity follow up study of BASF employees exposed to 2,3,7, 8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

57. Zober, A., P. Messerer, and P. Huber. 1990. Thirty-four-year mortality follow-up of BASF employees exposed to 2,3,7,8-TCDD after the 1953 accident. *International Archives of Occupational and Environmental Health* 62:139-57.

58. Kogan, M.D., and R.W. Clapp. 1985. Mortality among Vietnam veterans in Massachusetts, 1972-1983. Massachusetts Office of the Commissioner of Veterans Services, Agent Orange Program.

59. Anderson, H.A., L.P. Hanrahan, M. Jensen, D. Laurin, W.Y. Yick, and P. Wiegman. 1986. Wisconsin Vietnam veteran mortality study: Proportionate mortality ratio study results. Wisconsin Division of Health: Madison, WI.

60. Thomas, T.L., H.K. Kang, and N.A. Dalager. 1991. Mortality among women Vietnam veterans, 1973-1987. *American Journal of Epidemiology* 134:973-80.

61. U.S. Centers for Disease Control. 1987. Postservice mortality among Vietnam veterans. The Centers for Disease Control Vietnam experience study. *The Journal of the American Medical Association* 257:790-5.

62. Bullman, T.A., and H.K. Kang. 1996. The risk of suicide among wounded Vietnam veterans. *American Journal of Public Health* 86:662-7.

63. Eisen, S.A., J. Goldberg, W.R. True, and W.G. Henderson. 1991. A co-twin control study of the effects of the Vietnam War on the self-reported physical health of veterans. *American Journal of Epidemiology* 134:49-58.

64. Fett, M.J., J.R. Nairn, D.M. Cobbin, and M.A. Adena. 1987. Mortality among Australian conscripts of the Vietnam conflict era. II. Causes of death. *American Journal of Epidemiology* 125:878-84.

65. Michalek, J.E., W.H. Wolfe, and J.C. Miner. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. II. Mortality. *The Journal of the American Medical Association* 264:1832-6.

66. Michalek, J.E., N.S. Ketchum, and F.Z. Akhtar. 1998. Postservice mortality of US Air Force veterans occupationally exposed to herbicides in Vietnam: 15-year follow-up. *American Journal of Epidemiology* 148:786-92.

67. O'Toole, B.I., R.P. Marshall, D.A. Grayson, R.J. Schureck, M. Dobson, M. Ffrench, B. Pulvertaft, L. Meldrum, J. Bolton, and J. Vennard. 1996. The Australian Vietnam Veterans Health Study: II. Self-reported health of veterans compared with the Australian population. *International Journal of Epidemiology* 25:319-30.

68. Stellman, S.D., J.M. Stellman, and J.F. Sommer, Jr. 1988. Health and reproductive outcomes among American Legionnaires in relation to combat and herbicide exposure in Vietnam. *Environmental Research* 47:150-74.

69. Thomas, T.L., and H.K. Kang. 1990. Mortality and morbidity among Army Chemical Corps Vietnam veterans: A preliminary report. *American Journal of Industrial Medicine* 18:665-73.

70. U.S. Centers for Disease Control. 1988. Health status of Vietnam veterans. II. Physical Health. The Centers for Disease Control Vietnam experience study. *The Journal of the American Medical Association* 259:2708-14.

71. Watanabe, K.K., and H.K. Kang. 1996. Mortality patterns among Vietnam veterans: A 24-year retrospective analysis. *Journal of Occupational and Environmental Medicine* 38:272-8.

72. Wolfe, W.H., J.E. Michalek, J.C. Miner, A. Rahe, J. Silva, W.F. Thomas, W.D. Grubbs, M.B. Lustik, T.G. Karrison, R.H. Roegner, and D.E. Williams. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. I. Physical health. *The Journal of the American Medical Association* 264:1824-31.

73. Wolfe, W.H., G.D. Lathrop, R.A. Albanese, and P.M. Moynahan. 1985. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides and associated dioxins. *Chemosphere* 14:707-16.

74. Wolfe, W.H., J.E. Michalek, J.C. Miner, R.H. Roegner, W.D. Grubbs, M.B. Lustik, A.S. Brockman, S.C. Henderson, and D.E. Williams. 1992. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides, serum dioxin analysis of 1987 examination results. *Chemosphere* 25: 213-6.

75. Kim, J.S., H.S. Lim, S.I. Cho, H.K. Cheong, and M.K. Lim. 2003. Impact of Agent Orange exposure among Korean Vietnam veterans. *Industrial Health* 41:149-57.

76. Coggon, D., B. Pannett, P.D. Winter, E.D. Acheson, and J. Bonsall. 1986. Mortality of workers exposed to 2 methyl-4 chlorophenoxyacetic acid. *Scandinavian Journal of Work, Environment and Health* 12:448-54.

77. Fingerhut, M.A., W.E. Halperin, D.A. Marlow, L.A. Piacitelli, P.A. Honchar, M.H. Sweeney, A.L. Greife, P.A. Dill, K. Steenland, and A.J. Suruda. 1991. Cancer mortality in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *New England Journal of Medicine* 324:212-8.

78. Roegner, R.H., W.D. Grubbs, M.B. Lustik, A.S. Brockman, S.C. Henderson, D.E. Williams, W.H. Wolfe, J.E. Michalek, and J.C. Miner. 1990. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

79. Grubbs, W.D., W.H. Wolfe, J.E. Michalek, D.E. Williams, M.B. Lustik, A.S. Brockman, S.C. Henderson, F.R. Burnett, R.G. Land, D.J. Osborne, V.K. Rocconi, M.E. Schreiber, J.C. Miner, G.L. Henriksen, and J.A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1992 followup examination results. NTIS: AD A 304 306, 304 308-316. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

80. Michalek, J.E., B.R. Burnham, H.E. Marden, Jr., J.N. Robinson, V.V. Elequin, J.C. Miner, R.W. Ogershok, W.K. Sneddon, W.D. Grubbs, B.C. Cooper, R.G. Land, V.K. Rocconi, M.E. Yeager, D.E. Williams, and M.E.B. Owens. 2000. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1997 follow-up examination results. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

81. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline morbidity study results. NTIS: AD A 138 340. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

82. Lathrop, G.D., S.G. Machado, T.G. Karrison, W.D. Grubbs, W.F. Thomas, W.H. Wolfe, J.E. Michalek, J.C. Miner, and M.R. Peterson. 1987. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188 262. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

83. Institute of Medicine. 1994. Health effects of herbicides used in Vietnam. National Academy Press: Washington, DC.

84. Institute of Medicine. 1997. Veterans and Agent Orange: Update 1996. National Academy Press: Washington, DC.

85. Institute of Medicine. 1999. Veterans and Agent Orange: Update 1998. National Academy Press: Washington, DC.

86. Institute of Medicine. 2001. Veterans and Agent Orange: Update 2000. National Academy Press: Washington, DC.

87. Institute of Medicine. 2003. Veterans and Agent Orange: Update 2002. National Academy Press: Washington DC.

88. Wolfe, W.H., J.E. Michalek, and J.C. Miner. 1994. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Mortality update—1994. Epidemiologic Research Division, Armstrong Laboratory, Human Systems Center, Brooks Air Force Base, TX.

89. Garrow, J.S., and J. Webster. 1985. Quetelet's index (W/H^2) as a measure of fatness. *International Journal of Obesity* 9:147-53.

90. Saito, I., A.R. Folsom, F.L. Brancati, B.B. Duncan, L.E. Chambless, and P.G. McGovern. 2000. Nontraditional risk factors for coronary heart disease incidence among persons with diabetes: The atherosclerosis risk in communities (ARIC) study. *Annals of Internal Medicine* 133(2):81-91.

91. Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L. R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

92. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57(6):369-78.

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16 HEMATOLOGY ASSESSMENT

16.1 INTRODUCTION

16.1.1 Background

16.1.1.1   Organs/Diseases

The Air Force Health Study (AFHS) hematology assessment included data from the laboratory examination. Fourteen hematologic variables were examined, including red blood cell (RBC) count, white blood cell (WBC) count, hemoglobin, hematocrit, and platelet count. The following absolute WBC counts were examined: segmented neutrophils, neutrophilic bands, lymphocytes, monocytes, eosinophils, and basophils. Fibrinogen, erythrocyte sedimentation rate (ESR), and RBC morphology were also analyzed.

Several chemical substances, including acetone, acrolein, zinc, acrylonitrile, 1,2-dichloroethene, benzene, and dinitrotoluene have been identified as affecting the hematologic system (1). This chapter discusses findings primarily related to blood cells and platelet counts. Hematologic malignancies are discussed in Chapter 10, while results of blood chemistry tests related to gastrointestinal function are summarized in Chapter 13.

16.1.1.2   Toxicology

Experiments in laboratory animals demonstrated that 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin) is directly toxic to the hematopoietic system in several species, although the toxic effects vary depending on the dosage and type of animal species. In many reports, it was difficult to distinguish primary from secondary effects of systemic toxicity.

In one study, dioxin administered to monkeys in low doses by oral gavage resulted in elevated neutrophil counts, while higher doses were associated with lymphocytopenia and thrombocytopenia (2). A decrease in overall cellularity and an increase in the myeloid-erythroid ratio were noted in approximately half of the sternal bone marrow samples examined at the conclusion of the experiment. One study in rats using a range of gavage dioxin doses reported depressed RBC counts and packed cell volumes in the high-dose group (3). Another rat experiment that administered even greater dioxin doses orally found elevated erythrocyte, reticulocyte, and neutrophil counts, with a reduction in mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), platelet counts, and clot retraction times. Authors Weissberg and Zinkl commented that these effects could be attributed to systemic toxicity with terminal dehydration (4). In a multispecies study, mice and guinea pigs given a wide range of dioxin orally were found to have dose-dependent reductions in leukocytes with relative lymphocytopenia within 1 week of dioxin administration, with thrombocytopenia and hemoconcentration occurring in rats (5). Several other animal experiments, although designed primarily to investigate immunologic sequelae of dioxin exposure, focused on selected hematologic elements, particularly macrophages and polymorphonuclear leukocytes. Whether the responses observed were secondary to inflammation or specific to dioxin is not known (4, 6-8).

Additional animal research relevant to the hematopoietic system focused on the altered cellular differentiation associated with dioxin toxicity. In mice, progenitor cells were suppressed following

exposure to dioxin in doses as low as 1.0 µg/kg of body weight, and in vitro studies demonstrated that myelotoxicity occurs by a direct inhibition of proliferating stem cells (9). A subsequent study from the same laboratory demonstrated a direct effect of dioxin on cultured lymphocytes resulting in a selective inhibition of B-cell differentiation into antibody-secretive cells (10). In these and other studies, evidence for the role of the aryl hydrocarbon (Ah) receptor in mediating these myelotoxic and lymphotoxic effects was found (11); however, the relevance of these observations to dioxin hematopoietic toxicity remains to be demonstrated in humans (12).

16.1.1.3   *Epidemiology*

In general, human observational studies have shown fewer and less consistent hematologic findings than the animal experiments. Mortality and morbidity studies including hematologic data as endpoints have been based on populations exposed to dioxin through environmental contamination (13-26), occupation (27-44), and during military service in Southeast Asia (SEA) (45-55).

16.1.1.3.1   *Epidemiology: Blood Chemistry Levels*

One of the most severe human environmental exposures to dioxin occurred consequent to an industrial explosion in Seveso, Italy, in 1976. Several medical surveillance reports monitored this heavily exposed population (13-18, 21, 22). According to laboratory tests, no differences in pathological conditions between exposed people and unexposed controls were reported (22). A morbidity study of workers involved in the cleanup of the Seveso environs found no differences in selected hematologic indices (hemoglobin, WBC count, and platelets) between exposed subjects and controls (14).

Several studies were conducted on populations environmentally exposed to dioxin through contaminated soil in the Quail Run (19, 20, 23) and Times Beach (25) residential areas of Missouri. No differences were found in any of the hematologic parameters examined, except for in the Times Beach study, which found a statistically significant increase in the mean platelet count in the exposed cohort relative to the unexposed. The difference, however, was not considered clinically meaningful (25). A follow-up study found no abnormalities in the complete blood count (CBC) related to the adipose tissue levels of dioxin (26).

Hematologic conditions were evaluated in relation to occupational dioxin exposure in several cohorts, including workers in the United States (27, 28, 32, 35, 39-41), Japan (56), Germany (34, 36), and other European countries (29-31, 33, 37, 38, 42, 57). Studies of dioxin-exposed chemical production workers in the United States generally found little indication for hematologic abnormalities (27, 32, 39, 41). In German populations of workers exposed to dioxin after a chemical accident (34) or during the production of resins (36), no differences between exposed subjects and controls were noted in WBC counts, platelet counts, or hemoglobin levels. Furthermore, no indication of hematologic effects was found in other European worker populations (31, 33, 37, 38) or in municipal waste incinerator workers chronically exposed to dioxins in Japan (56).

Studies of Vietnam veterans generally found little evidence for an association between dioxin exposure and hematologic abnormalities (45-54, 58-60). In the Vietnam Experience Study, results of hematologic tests revealed no difference in hemoglobin levels and WBC counts between Vietnam and non-Vietnam veterans (55). In a recent study of Korean Vietnam veterans, WBC counts were similar among veterans compared to non-veterans; however, hemoglobin levels were found to be reduced among veterans (59). Another study of Korean Vietnam veterans found no association between hematologic parameters and veteran status or level of Agent Orange exposure (60). Early investigations found hemoglobin levels to be elevated in the Ranch Hands as compared to the reference group, although this observation was not

considered to be clinically relevant (53). Furthermore, Ranch Hand participants were found to have slightly higher mean platelet counts and a greater percentage of abnormally high platelet counts than Comparisons (48, 49, 54). WBC counts showed associations with dioxin exposure consistent with a dose-response effect (54). Most recently, Ranch Hands with the highest serum dioxin levels had slightly elevated MCVs and platelet counts relative to veterans not involved in Operation Ranch Hand (51). These elevations, however, were determined to be of unknown clinical significance and may not have been related to dioxin exposure (51).

16.1.1.3.2   *Epidemiology: Diseases of Blood and Blood-forming Organs*

In the Seveso population, an increased risk of mortality from blood diseases was observed among residents classified as exposed (16, 18); however, none of the six cases occurred among those with the highest exposures (16). Occupational cohort studies in the United States and Europe found no evidence of an increased risk of mortality from diseases of the blood and blood-forming organs among dioxin-exposed workers (28, 35, 40, 42). One co-twin case-control study found no association between service in Vietnam and self-reported morbidity from blood disorders (45).

16.1.2   Summary of Previous Analyses of the Air Force Health Study

16.1.2.1   *1982 Baseline Examination Summary Results*

The functional integrity of the hematopoietic system was assessed at the 1982 baseline examination by the measurement of RBC count, WBC count, hemoglobin, hematocrit, MCV, MCH, mean corpuscular hemoglobin concentration (MCHC), platelet count, and ESR (analyzed as part of the General Health Assessment prior to 2002). These variables were analyzed in the discrete form to detect differences in the percentages of values outside the normal laboratory range, as well as analyzed in the continuous form to detect shifts in mean values between the Ranch Hand and Comparison groups.

The Ranch Hand group had a significantly higher adjusted mean MCV and MCH than the Comparison group (p=0.05 and p=0.04, respectively), although the magnitude of the difference was small in each case. The Ranch Hand adjusted mean values for RBC count, WBC count, hemoglobin, hematocrit, MCHC, and platelet count were not significantly different from the adjusted mean values of the Comparison group. The percent of abnormal values for these eight variables, as established by the upper and lower limits of normal, did not differ significantly between the two groups.

No overall differences in ESR were found, although a significant interaction between group and age for ESR was noted; younger Ranch Hands had fewer ESR abnormalities than did Comparisons, whereas no difference was found in participants older than 40.

16.1.2.2   *1985 Follow-up Examination Summary Results*

The same variables (i.e., RBC count, WBC count, hemoglobin, hematocrit, MCV, MCH, MCHC, platelet count, and ESR) were analyzed in the 1985 follow-up examination. The adjusted analyses of the discrete form of these variables showed no statistically significant difference between the Ranch Hand and Comparison groups.

As no subgroup demonstrated consistent patterns of hematologic impairment, biologic relevance was not assigned to the interactions. The significant group differences found for MCV and MCH at the baseline examination were not present in the 1985 follow-up examination analyses. The covariate associations of

age, race, occupation, and lifetime smoking history were highly significant for many of the hematologic variables.

The geometric mean ESRs did not differ significantly between Ranch Hands and Comparisons after adjustment for age, race, occupation, personality score, and an age-by-personality score interaction. In the analysis of the discrete form of ESR, 5.8 percent of the Ranch Hands had ESR abnormalities (>20 mm/hour), contrasted to 3.6 percent in the Comparison group. This difference was significant after adjustment for age and personality score (p=0.011).

The longitudinal analyses of platelet count found a significant group difference, with the Ranch Hands having an average decrease in platelet count between the 1982 and 1985 examinations and the Comparisons having an average increase. As a result, the baseline group difference (nonsignificant) in mean values approached equality at the 1985 follow-up examination.

Longitudinal differences between the 1982 baseline and the 1985 follow-up examination were also observed for ESR. The analysis revealed a highly significant group difference (p=0.002) because of a reversal of findings between examinations (i.e., a significant adverse association in the [younger] Comparisons at the baseline examination versus a significant adverse association in the Ranch Hands at the follow-up examination).

16.1.2.3 1987 Follow-up Examination Summary Results

The hematologic status of the Ranch Hand and Comparison groups was assessed by the examination of RBC count, WBC count, hemoglobin, hematocrit, MCV, MCH, MCHC, platelet count, and ESR. There were no statistically significant differences between the Ranch Hand and Comparison groups for mean RBC count, hemoglobin, hematocrit, MCV, MCH, and MCHC in analyses adjusted for the covariates of age, race, occupation, current cigarette smoking, and lifetime cigarette smoking history.

Mean platelet counts were significantly greater in Ranch Hands than in Comparisons, as was the percentage of individuals with abnormally high platelet counts. There was little difference in the geometric mean values of ESR in the two groups, but Ranch Hands had a significantly higher percentage of individuals with an abnormal ESR (>20 mm/hour) than Comparisons. Only three participants (two Ranch Hands and one Comparison) were found to have rates in excess of 100 mm/hour; one of these (a Comparison) proved to have lung cancer and died in early 1989. No diagnosis was established for either of the two Ranch Hands during the course of the 1987 examination.

Longitudinal analyses detected a significantly greater decrease in the mean platelet count in Ranch Hands than in Comparisons, despite the higher overall mean count, from the baseline examination to the 1987 follow-up examination. For ESR, there was a significant difference between groups in the change from baseline to the 1987 follow-up examination, with a relatively greater number of Ranch Hands than Comparisons shifting from normal at baseline to abnormal at the follow-up examination.

16.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Examination Summary Results

Hemoglobin and hematocrit were positively associated with dioxin levels in 1987 when time since duty in SEA was no more than 18.6 years and inversely associated with dioxin levels in 1987 when time since duty in SEA was greater than 18.6 years. For the discrete RBC count analysis, the relative risk of an abnormally low count was less than one when time since duty in SEA did not exceed 18.6 years and was greater than one when time since duty in SEA was more than 18.6 years. Because a low RBC count was

considered abnormal for the purpose of these statistical analyses, the trend in relation to 1987 dioxin was similar to that in the analyses of the continuous form of hemoglobin and hematocrit.

In the analysis of the discrete form of prothrombin time, the trend in relation to 1987 dioxin also was similar to that in the analyses of the continuous form of hemoglobin and hematocrit. In the categorized dioxin analyses, whenever the overall contrast showed significant differences among the categories, the mean level or percent abnormal in the three categories of Ranch Hands (i.e., officers, enlisted flyers, and enlisted groundcrew) tended to exceed the corresponding mean level or percent abnormal in the background category that consisted of Comparisons.

ESR exhibited a significant positive association with initial dioxin. The analyses for the four dioxin categories overall exhibited significant contrasts for ESR, and the high versus background contrast and the low versus background contrast were significant with the Ranch Hands exceeding Comparisons.

The longitudinal analyses of MCV, MCH, and platelet count displayed no significant associations with dioxin. In the longitudinal analyses of ESR, the percentages of abnormalities in 1987 were greater for Ranch Hands in the low dioxin category and in the high dioxin category than for Comparisons.

In summary, the results of the previous analysis revealed no meaningful association between hematopoietic toxicity and dioxin. Statistical analyses of WBC count, platelet count, and ESR raised the possibility of subtle biologic effects that cannot be considered clinically meaningful, but did point to the need for follow-up in future AFHS examinations. The increased platelet and WBC counts, in addition to the elevation of ESRs, were thought to indicate the presence of a chronic inflammatory response to dioxin.

16.1.2.5 1992 Follow-up Examination Summary Results

The statistical analyses of MCV, MCH, and MCHC were eliminated for the 1992 follow-up examination and RBC morphology (normal, abnormal), absolute neutrophils (segs), absolute neutrophils (bands), absolute lymphocytes, absolute monocytes, absolute eosinophils, and absolute basophils were added. In the analyses of these variables, platelet count exhibited significant associations with the herbicide exposure indices. Ranch Hands in the enlisted flyer and enlisted groundcrew categories displayed statistically significant higher mean platelet counts than Comparisons. Analyses using extrapolated levels of initial dioxin showed that Ranch Hands with high dioxin levels had significantly greater mean platelet count measurements than Comparisons. ESR also displayed a significant positive association with 1987 dioxin levels. The 1992 follow-up examination results supported the results found in both the 1987 follow-up examination and in the serum dioxin analysis of the 1987 follow-up examination, but the biologic meaning was uncertain.

16.1.2.6 1997 Follow-up Examination Summary Results

In the analyses of hematologic variables for the 1997 follow-up examination, which mirrored the variables studied for the 1992 follow-up examination, platelet count exhibited significant dose-response associations with the indices of dioxin. Ranch Hand enlisted flyers and groundcrew exhibited slightly but significantly higher mean platelet counts than did Comparisons. Ranch Hands in the high dioxin category also exhibited a significantly higher mean platelet count than Comparisons. No differences in the percentages of abnormal ESRs between Ranch Hands and Comparisons or relations between abnormal ESRs and dioxin levels were observed during the 1997 examination. ESRs increased as 1987 dioxin levels increased.

Longitudinal analyses showed that Ranch Hands, particularly the two enlisted strata, had an increased percentage of abnormal ESRs than did Comparisons over the 15 years of the study since 1982. These analyses also showed that the percentages of abnormalities increased from 1982 to 1997 as dioxin levels increased. This positive association raises the possibility of a subtle inflammatory, infectious, or occult malignant disease process related to the body burden of dioxin.

In general, the results in the 1997 follow-up examination paralleled the findings of the 1987 and 1992 follow-up examinations.

16.1.3 Parameters for the 2002 Hematology Assessment

16.1.3.1 Dependent Variables

The analysis of the hematology assessment consisted of data from the laboratory examination only. No questionnaire or physical examination data were analyzed.

16.1.3.1.1 Laboratory Variables

A total of 14 hematology variables investigated as part of the 2002 laboratory follow-up examination were analyzed statistically. A CBC with a differential WBC count was performed with the differential results reported as absolute counts. Elements of the CBC that were analyzed were RBC count, WBC count, hemoglobin, hematocrit, platelet count, and the following absolute WBC counts: segmented neutrophils, neutrophilic bands, lymphocytes, monocytes, eosinophils, and basophils. Lymphocytes included both reactive and nonreactive lymphocytes. RBC morphology was noted as normal or abnormal. In addition, measurements for ESR and fibrinogen were collected. These variables were determined by routine hematologic procedures. In particular, the cell counts were performed on the Abbott Cell-Dyn 4000® automated instrument, and fibrinogen was measured on the Dade-Behring Blood Coagulation System instrument. The ESR was performed using Vesmatic™ equipment. All dependent variables were analyzed in the continuous form, except for the RBC morphology, which was analyzed as discrete only. ESR and fibrinogen were analyzed continuously and in their discrete forms using Scripps Clinic normal ranges as cutpoints. RBC count, WBC count, hemoglobin, hematocrit, and platelet count were analyzed as continuous and were trichotomized as abnormal low, normal, and abnormal high.

RBC morphology was constructed from a number of laboratory conditions, many of which were minor abnormalities. Participants having at least one of the following conditions at the 2002 follow-up examination were considered to be abnormal for RBC morphology: acanthocytes, rouleaux, Burr cells, spherocytes, moderate microcytes, many microcytes, moderate macrocytes, moderate amount of ovalocytes, hypochromia, anisocytosis, polychromasia, slight baso-stippling, few target cells, Howell-Jolly bodies, and few teardrop cells. Participants with only few ovalocytes, few microcytes, or few macrocytes were considered to be normal for RBC morphology.

Absolute neutrophils (bands), absolute eosinophils, and absolute basophils had a large number of measurements equal to 0 counts per mm³. The nonzero measurements exhibited a positively skewed distribution, so a logarithmic transformation was applied to achieve an approximate normal distribution. The logarithmic transformation, however, could not be applied to the measurements equal to 0 counts per mm³. Consequently, these variables were analyzed in two forms: (1) an analysis of the nonzero measurements and (2) an analysis of the proportion of zero measurements.

Participants with a fever (body temperature greater than or equal to 100 degrees Fahrenheit) at the time of the examination or testing positive for the human immunodeficiency virus (HIV) were excluded from the

analysis of all variables. Participants whose platelet count was inexact because of clumping of the platelets were excluded from the analysis of platelet count.

16.1.3.2 Covariates

Age, race, military occupation, current level of cigarette smoking (cigarettes/day), lifetime cigarette smoking history (pack-years), and body mass index (kg/m^2) were used as covariates in adjusted statistical analyses evaluating the hematologic dependent variables. Age, race, and military occupation were determined from military records. The covariates current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 2002 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

Body mass index was calculated as weight/(height)^2, where the weight was measured in kilograms and the height was measured in meters at the physical examination (61). For purposes of covariate associations for discrete dependent variables, body mass index was dichotomized as "not obese" (≤ 30 kg/m^2) and "obese" (>30 kg/m^2).

16.1.4 Statistical Methods

Table 16-1 summarizes the statistical analysis performed for the 2002 hematology assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, exclusions, and statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 16-1.

Table 16-1. Statistical Analysis for the Hematology Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
RBC Count (million/mm^3)	LAB	C/D	Abnormal Low: <4.3 Normal: 4.3–5.9 Abnormal High: >5.9	(1)	(a)	U:PR,CS,GLM,TT A:PR,GLM
WBC Count (thousand/mm^3)	LAB	C/D	Abnormal Low: <4.5 Normal: 4.5–11.0 Abnormal High: >11.0	(1)	(a)	U:PR,CS,GLM,TT A:PR,GLM
Hemoglobin (gm/dL)	LAB	C/D	Abnormal Low: <13.9 Normal: 13.9–18.0 Abnormal High: >18.0	(1)	(a)	U:PR,CS,GLM,TT A:PR,GLM
Hematocrit (percent)	LAB	C/D	Abnormal Low: <39.0 Normal: 39.0–55.0 Abnormal High: >55.0	(1)	(a)	U:PR,CS,GLM,TT A:PR,GLM
Platelet Count (thousand/mm^3)	LAB	C/D	Abnormal Low: <130 Normal: 130–400 Abnormal High: >400	(1)	(b)	U:PR,CS,GLM,TT A:PR,GLM

Table 16-1. Statistical Analysis for the Hematology Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
RBC Morphology	LAB	D	Abnormal Normal	(1)	(a)	U:LR,CS A:LR
Absolute Neutrophils (segs) (thousand/mm^3)	LAB	C	--	(1)	(a)	U:GLM,TT A:GLM
Absolute Neutrophils (bands) (thousand/mm^3)	LAB	C/D	Zero Nonzero	(1)	(a)	U:LR,CS,GLM,TT A:LR,GLM
Absolute Lymphocytes (thousand/mm^3)	LAB	C	--	(1)	(a)	U:GLM,TT A:GLM
Absolute Monocytes (thousand/mm^3)	LAB	C	--	(1)	(a)	U:GLM,TT A:GLM
Absolute Eosinophils (thousand/mm^3)	LAB	C/D	Zero Nonzero	(1)	(a)	U:LR,CS,GLM,TT A:LR,GLM
Absolute Basophils (thousand/mm^3)	LAB	C/D	Zero Nonzero	(1)	(a)	U:LR,CS,GLM,TT A:LR,GLM
Fibrinogen (mg/dL)	LAB	C/D	High: >450 Normal: ≤450	(1)	(a)	U:LR,CS,GLM,TT A:LR,GLM
Erythrocyte Sedimentation Rate (ESR) (mm/hour)	LAB	C/D	Abnormal: >20 Normal: ≤20	(1)	(a)	U:LR,CS,GLM,TT A:LR,GLM

[a]Covariates:

(1) age, race, military occupation, current cigarette smoking, lifetime cigarette smoking history, body mass index.

[b]Exclusions:

(a) participants with body temperatures greater than or equal to 100 degrees Fahrenheit, participants testing positive for HIV.

(b) participants with body temperatures greater than or equal to 100 degrees Fahrenheit, participants testing positive for HIV, participants whose platelet count was inexact because of clumping of the platelets.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	C/D	Born ≥1942 Born <1942
Race	MIL	D	Black Non-Black
Military Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew

Table 16-1. Statistical Analysis for the Hematology Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints
Current Cigarette Smoking (cigarettes/day)	Q-SR	C/D	Never Former >0–20 >20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	C/D	0 >0–10 >10
Body Mass Index (kg/m^2)	PE	C/D	Not Obese: ≤30 Obese: >30

Abbreviations

Data Source:
LAB: 2002 laboratory results
MIL: Air Force military records
PE: 2002 physical examination
Q-SR: 2002 AFHS health questionnaire (self-reported)

Data Form:
C: Continuous form of dependent variable
D: Discrete form of dependent variable or covariate
C/D: Continuous and discrete forms of dependent variable; appropriate form for analysis (either continuous or discrete) of covariate

Statistical Analysis:
U: Unadjusted analysis
A: Adjusted analysis

Statistical Methods:
CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
GLM: General linear models analysis
LR: Logistic regression analysis
PR: Polytomous logistic regression analysis
TT: Two-sample t-test

Four models were examined for each dependent variable given in Table 16-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for covariates. These covariates are given in Table 16-1. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. In an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-4, the median level of exposure to dioxin was highest for enlisted groundcrew, followed by enlisted flyers, then officers.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the CDC using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in parts per trillion (ppt) on a lipid weight basis (62). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2. A statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model to account for body mass index-related differences in elimination rate (63).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. Another category was examined by combining the low and high Ranch Hand categories. This combination is referred to in the tables as the "low plus high Ranch Hand" category. These five categories—Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the four Ranch Hand categories and the dependent variable in the Comparison category was examined. As in Model 2, a statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables. One Ranch Hand without a dioxin measure was excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The term "unadjusted" was used in the text and tables as follows: Models 1 and 4 did not adjust for any covariates. Models 2 and 3 adjusted only for body mass index at the time of the blood measurement for dioxin. The term "adjusted" was used in the text and tables as follows: Models 1 and 4 adjusted for the covariates shown in Table 16-1 unless otherwise specified by a footnote to the table. Models 2 and 3 additionally adjusted only for body mass index at the time of the blood measurement for dioxin.

Table 16-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants that were excluded from analyses is given.

Table 16-2. Number of Participants Excluded or with Missing Data for the Hematology Assessment

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Fibrinogen	DEP	1	0	0	1	1	0
Current Cigarette Smoking	COV	0	2	0	0	0	2
Lifetime Cigarette Smoking History	COV	0	3	0	0	0	3
Body Mass Index	COV	1	0	0	1	1	0
Platelet Clumping	EXC	1	3	0	1	1	3
Fever at the Time of the Physical Examination	EXC	3	1	2	3	3	1
HIV Positive	EXC	3	2	3	3	3	2

[a]777 Ranch Hands and 1,174 Comparisons for group.
[b]424 Ranch Hands for initial dioxin; 776 Ranch Hands for 1987 dioxin.
[c]776 Ranch Hands and 1,174 Comparisons for categorized dioxin.

Note: DEP = Dependent variable.
      COV = Covariate.
      EXC = Exclusion.

16.2   RESULTS

16.2.1 Dependent Variable-covariate Associations

The complete results of covariate associations with each hematologic dependent variable are documented in Appendix F, Table F-8. These associations are pairwise between the dependent variable and the covariate and are not adjusted for any other covariates. The following paragraphs summarize the pattern of significant ($p \leq 0.05$) dependent variable-covariate associations.

Age was associated with RBC count, hemoglobin, hematocrit, fibrinogen, and ESR in both the discrete and continuous forms. RBC count, hemoglobin, and hematocrit decreased with increasing age, while fibrinogen and ESR increased with increasing age. Similarly, abnormally low RBC counts, hemoglobin levels, and hematocrit levels were seen more often in older participants, as were high fibrinogen levels and high ESRs. Platelet counts and absolute lymphocyte counts decreased as the age of the participants increased. Older participants were also more likely to have had an abnormal RBC morphology than younger participants.

Race was associated with the continuous form of WBC count, hemoglobin, hematocrit, platelet count, segmented neutrophils, neutrophilic bands, fibrinogen, and ESR. The mean WBC count, hemoglobin, hematocrit, and absolute neutrophils (segs and bands) were lower in Blacks than non-Blacks. Blacks had a higher mean platelet count, fibrinogen level, and ESR than non-Blacks.

The discrete form of RBC count, WBC count, hemoglobin, hematocrit, RBC morphology, neutrophilic bands, and fibrinogen was also associated with race. Black participants were more likely to have had an abnormally high RBC count than non-Black participants. Blacks were more than twice as likely, however, to have had abnormally low hemoglobin levels and hematocrit levels than non-Blacks. A higher percentage of Blacks had abnormally low WBC counts than non-Blacks. Blacks were more likely to have an abnormal RBC morphology, abnormally high fibrinogen levels, and no neutrophilic bands than non-Blacks.

The continuous form of RBC count, WBC count, hemoglobin, hematocrit, platelet count, fibrinogen, and ESR was associated with military occupation, as were absolute counts of segmented neutrophils, lymphocytes, monocytes, and eosinophils. The discrete form of RBC count, WBC count, and fibrinogen was also found to be associated with military occupation.

Officers were more likely to have had a lower mean RBC count, hemoglobin level, hematocrit, WBC count, platelet count, fibrinogen level, and ESR than enlisted flyers or enlisted groundcrew. Mean absolute counts of segmented neutrophils, lymphocytes, monocytes, and eosinophils were also lower in officers than in enlisted flyers or groundcrew. Fewer officers had abnormally high fibrinogen levels and abnormally high WBC counts than enlisted participants. Officers were more likely to have had abnormally low RBC counts than enlisted participants and were less likely to have had abnormally high RBC counts.

Current cigarette smoking was positively associated with RBC count, WBC count, hemoglobin, hematocrit, platelet count, fibrinogen, and absolute counts of segmented and banded neutrophils, lymphocytes, monocytes, eosinophils, and basophils. While the discrete form of RBC count, WBC count, hemoglobin, hematocrit, and fibrinogen varied with current cigarette smoking, no consistent positive association with current cigarette smoking was apparent.

WBC counts, fibrinogen, ESR, and absolute counts of segmented and banded neutrophils, lymphocytes, monocytes, eosinophils, and basophils increased as lifetime cigarette smoking increased. RBC counts decreased with increasing lifetime cigarette smoking. The heaviest smoker group (in terms of pack-years) had the highest percentage of participants with abnormally high WBC counts and the lowest percentage of participants with abnormally low WBC counts. The heaviest smokers also had the highest percentage of participants with abnormally low RBC counts and abnormally high fibrinogen levels.

Body mass index was positively correlated with RBC count, WBC count, absolute lymphocytes, monocytes, eosinophils, basophils, fibrinogen, and ESR. Platelet counts increased with decreasing body mass index. Fewer obese participants had abnormal low or abnormal high WBC counts than participants who were not obese. Obese participants were more likely to have had abnormally low platelet counts and less likely to have had abnormally high platelet counts than participants who were not obese.

16.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 16-1. Dependent variables were based on data from the Scripps Clinic laboratory, which were obtained during the 2002 physical examination.

16.2.2.1 Laboratory Variables

16.2.2.1.1 RBC Count (Continuous)

All unadjusted and adjusted results from the Model 1 through Model 4 analyses of RBC count in the continuous form were nonsignificant (Table 16-3(a–h): p>0.06 for each analysis).

Table 16-3. Analysis of RBC Count (million/mm³) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*4.98*	*0.00 (-0.04,0.04)*	*0.937*
	Comparison	*1,171*	*4.98*		
Officer	Ranch Hand	306	4.88	-0.01 (-0.08,0.05)	0.704
	Comparison	460	4.89		
Enlisted Flyer	Ranch Hand	133	4.98	-0.03 (-0.13,0.08)	0.600
	Comparison	185	5.01		
Enlisted Groundcrew	Ranch Hand	332	5.07	0.02 (-0.04,0.09)	0.505
	Comparison	526	5.05		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*4.98*	*0.00 (-0.05,0.04)*	*0.856*
	Comparison	*1,168*	*4.99*		
Officer	Ranch Hand	305	4.92	-0.01 (-0.08,0.06)	0.765
	Comparison	460	4.93		
Enlisted Flyer	Ranch Hand	133	5.01	-0.03 (-0.13,0.07)	0.597
	Comparison	185	5.04		
Enlisted Groundcrew	Ranch Hand	332	5.01	0.01 (-0.05,0.07)	0.737
	Comparison	523	5.00		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	139	4.98	4.98	0.001	0.010 (0.016)	0.560
Medium	143	5.01	5.01			
High	137	5.00	5.00			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 16-3. Analysis of RBC Count (million/mm^3) (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	139	5.03	0.083	-0.032 (0.019)	0.090
Medium	143	4.99			
High	137	4.92			

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,171	4.98	4.98		
Background RH	351	4.95	4.96	-0.02 (-0.08,0.03)	0.391
Low RH	210	5.00	4.99	0.01 (-0.05,0.08)	0.685
High RH	209	5.00	5.00	0.02 (-0.05,0.09)	0.587
Low plus High RH	419	5.00	5.00	0.02 (-0.04,0.07)	0.532

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,168	4.99		
Background RH	350	5.00	0.01 (-0.04,0.07)	0.670
Low RH	210	5.00	0.02 (-0.05,0.09)	0.597
High RH	209	4.92	-0.07 (-0.13,0.00)	0.062
Low plus High RH	419	4.96	-0.02 (-0.08,0.03)	0.365

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-3. Analysis of RBC Count (million/mm^3) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean**	**R^2**	**Slope (Standard Error)**	**p-Value**
Low	259	4.94	0.003	0.016 (0.011)	0.130
Medium	257	4.98			
High	254	5.01			

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	258	5.06	0.085	-0.020 (0.012)	0.099
Medium	257	5.06			
High	254	4.98			

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

16.2.2.1.2 RBC Count (Discrete)

No significant associations were observed between exposure groups or dioxin levels in the unadjusted and adjusted Model 1 through Model 4 analyses of the discrete form of RBC count (Table 16-4(a–h): p>0.15 for each analysis).

Table 16-4. Analysis of RBC Count (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal Unadjusted Relative Risk (95% C.I.)	p-Value	Abnormal High vs. Normal Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*56 (7.3)*	*698 (90.5)*	*17 (2.2)*	*1.00 (0.70,1.42)*	*0.990*	*0.89 (0.48,1.63)*	*0.700*
	Comparison	*1,171*	*85 (7.3)*	*1,057 (90.3)*	*29 (2.5)*				
Officer	Ranch Hand	306	32 (10.5)	269 (87.9)	5 (1.6)	1.11 (0.69,1.80)	0.667	1.53 (0.44,5.33)	0.506
	Comparison	460	44 (9.6)	411 (89.3)	5 (1.1)				
Enlisted Flyer	Ranch Hand	133	9 (6.8)	121 (91.0)	3 (2.3)	0.94 (0.39,2.27)	0.887	0.51 (0.13,1.96)	0.325
	Comparison	185	13 (7.0)	164 (88.6)	8 (4.3)				
Enlisted Groundcrew	Ranch Hand	332	15 (4.5)	308 (92.8)	9 (2.7)	0.84 (0.44,1.60)	0.591	0.88 (0.38,2.02)	0.763
	Comparison	526	28 (5.3)	482 (91.6)	16 (3.0)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Abnormal Low vs. Normal Adjusted Relative Risk (95% C.I.)	p-Value	Abnormal High vs. Normal Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,938*	*1.00 (0.70,1.43)*	*0.995*	*0.85 (0.46,1.57)*	*0.599*
Officer	765	1.14 (0.70,1.86)	0.608	1.50 (0.43,5.25)	0.522
Enlisted Flyer	318	0.90 (0.37,2.21)	0.823	0.48 (0.12,1.84)	0.282
Enlisted Groundcrew	855	0.85 (0.44,1.64)	0.627	0.84 (0.36,1.94)	0.676

Table 16-4. Analysis of RBC Count (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics					Analysis Results for Log$_2$ (Initial Dioxin)[a]			
			Number (%)		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]	p-Value
Low	139	8 (5.8)	130 (93.5)	1 (0.7)	0.93 (0.68,1.26)	0.622	1.06 (0.65,1.74)	0.807
Medium	143	9 (6.3)	130 (90.9)	4 (2.8)				
High	137	8 (5.8)	125 (91.2)	4 (2.9)				

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)				
	Abnormal Low vs. Normal			Abnormal High vs. Normal	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value		Adjusted Relative Risk (95% C.I.)[a]	p-Value
419	1.11 (0.81,1.54)	0.511		1.12 (0.67,1.88)	0.659

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for military occupation because of the sparse number of Ranch Hands with an abnormally high RBC count.

Table 16-4. Analysis of RBC Count (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

| Dioxin Category | n | Number (%) | | | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
		Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	85 (7.3)	1,057 (90.3)	29 (2.5)				
Background RH	351	31 (8.8)	312 (88.9)	8 (2.3)	1.29 (0.84,2.00)	0.245	0.95 (0.43,2.12)	0.905
Low RH	210	12 (5.7)	193 (91.9)	5 (2.4)	0.76 (0.41,1.42)	0.394	0.94 (0.36,2.46)	0.898
High RH	209	13 (6.2)	192 (91.9)	4 (1.9)	0.81 (0.44,1.48)	0.490	0.75 (0.26,2.15)	0.589
Low plus High RH	419	25 (6.0)	385 (91.9)	9 (2.1)	0.78 (0.49,1.25)	0.305	0.84 (0.39,1.80)	0.649

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

| Dioxin Category | n | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
		Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168				
Background RH	350	1.14 (0.72,1.79)	0.575	1.06 (0.46,2.42)	0.895
Low RH	210	0.70 (0.37,1.32)	0.266	0.84 (0.31,2.22)	0.719
High RH	209	1.20 (0.63,2.30)	0.578	0.62 (0.21,1.81)	0.382
Low plus High RH	419	0.91 (0.56,1.48)	0.715	0.72 (0.33,1.55)	0.402

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-4. Analysis of RBC Count (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

| 1987 Dioxin Category Summary Statistics | | | | | Analysis Results for Log$_2$ (1987 Dioxin)[a] | | | |
| | | Number (%) | | | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	22 (8.5)	233 (90.0)	4 (1.5)	0.88 (0.74,1.05)	0.152	1.06 (0.79,1.42)	0.708
Medium	257	19 (7.4)	233 (90.7)	5 (1.9)				
High	254	15 (5.9)	231 (90.9)	8 (3.1)				

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (1987 Dioxin) | | | | |
| | Abnormal Low vs. Normal | | Abnormal High vs. Normal | | |
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value	
769	0.98 (0.78,1.24)	0.882	1.04 (0.73,1.48)	0.824	

[a]Relative risk for a twofold increase in 1987 dioxin.

16.2.2.1.3 WBC Count (Continuous)

No significant associations between exposure group or dioxin levels and WBC count were observed in Model 1 through Model 3 unadjusted and adjusted analyses (Table 16-5(a–f): p>0.06 for each analysis), and no association between 1987 dioxin levels and WBC counts was seen in the unadjusted analysis of Model 4 (Table 16-5(g): p=0.341). After adjustment for the covariates, however, the WBC count significantly decreased as the 1987 dioxin levels increased (Table 16-5(h): Adjusted Slope=-0.014, p=0.047). The adjusted mean WBC count for the low 1987 dioxin category was 5.98 thousand cells per mm^3 compared to 5.81 thousand cells per mm^3 for the medium category and 5.83 thousand cells per mm^3 for the high category.

16.2.2.1.4 WBC Count (Discrete)

No significant associations with exposure group and dioxin were seen in Model 1, Model 2, or Model 3 unadjusted and adjusted analyses of WBC count in its discrete form (Table 16-6(a-f): p>0.10 for each contrast).

A significant inverse relation was seen between 1987 dioxin levels and abnormally high WBC counts in the unadjusted and adjusted Model 4 analyses (Table 16-6(g, h): Unadjusted Relative Risk [RR]=0.65, p=0.011; Adjusted RR=0.61, p=0.005). The percentage of Ranch Hands with an abnormally high WBC count was 2.7 percent in the low 1987 dioxin category, 1.9 percent in the medium category, and 1.6 percent in the high category.

Table 16-5. Analysis of WBC Count (thousand/mm^3) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*771*	*6.24*	*0.12*	*0.141*
	Comparison	*1,171*	*6.12*		
Officer	Ranch Hand	306	5.91	0.03	0.826
	Comparison	460	5.88		
Enlisted Flyer	Ranch Hand	133	6.37	0.24	0.221
	Comparison	185	6.13		
Enlisted Groundcrew	Ranch Hand	332	6.51	0.17	0.171
	Comparison	526	6.33		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*770*	*5.91*	*0.07*	*0.359*
	Comparison	*1,168*	*5.84*		
Officer	Ranch Hand	305	5.71	0.02	0.883
	Comparison	460	5.69		
Enlisted Flyer	Ranch Hand	133	5.92	0.16	0.375
	Comparison	185	5.76		
Enlisted Groundcrew	Ranch Hand	332	6.13	0.08	0.484
	Comparison	523	6.05		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	139	6.11	6.12	0.009	0.012 (0.010)	0.210
Medium	143	6.57	6.58			
High	137	6.26	6.25			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of WBC count versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	5.79	0.183	-0.001 (0.010)	0.901
Medium	143	6.00			
High	137	5.70			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of WBC count versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 16-5. Analysis of WBC Count (thousand/mm³) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,171	6.12	6.12		
Background RH	351	6.14	6.16	0.04	0.691
Low RH	210	6.26	6.25	0.13	0.297
High RH	209	6.37	6.35	0.23	0.079
Low plus High RH	419	6.32	6.30	0.18	0.065

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,168	5.84		
Background RH	350	5.94	0.10	0.324
Low RH	210	5.91	0.07	0.534
High RH	209	5.83	-0.01	0.913
Low plus High RH	419	5.87	0.03	0.739

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-5. Analysis of WBC Count (thousand/mm³) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	259	6.14	0.001	0.006 (0.006)	0.341
Medium	257	6.12			
High	254	6.45			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of WBC count versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	258	5.98	0.151	-0.014 (0.007)	0.047*
Medium	257	5.81			
High	254	5.83			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of WBC count versus log_2 (1987 dioxin).

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 16-6. Analysis of WBC Count (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
			Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)	p-Value	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*74 (9.6)*	*681 (88.3)*	*16 (2.1)*	*0.86 (0.64,1.17)*	*0.341*	*0.92 (0.49,1.73)*	*0.793*
	Comparison	*1,171*	*128 (10.9)*	*1,017 (86.8)*	*26 (2.2)*				
Officer	Ranch Hand	306	31 (10.1)	272 (88.9)	3 (1.0)	0.79 (0.50,1.26)	0.324	0.62 (0.16,2.43)	0.497
	Comparison	460	57 (12.4)	396 (86.1)	7 (1.5)				
Enlisted Flyer	Ranch Hand	133	19 (14.3)	108 (81.2)	6 (4.5)	1.26 (0.65,2.45)	0.488	1.76 (0.52,5.90)	0.363
	Comparison	185	22 (11.9)	158 (85.4)	5 (2.7)				
Enlisted Groundcrew	Ranch Hand	332	24 (7.2)	301 (90.7)	7 (2.1)	0.75 (0.45,1.25)	0.276	0.77 (0.31,1.93)	0.575
	Comparison	526	49 (9.3)	463 (88.0)	14 (2.7)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Adjusted Relative Risk (95% C.I.)	p-Value	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,938*	*0.89 (0.65,1.21)*	*0.463*	*0.84 (0.44,1.60)*	*0.598*
Officer	765	0.79 (0.50,1.27)	0.330	0.62 (0.16,2.42)	0.490
Enlisted Flyer	318	1.34 (0.68,2.66)	0.395	1.50 (0.44,5.13)	0.518
Enlisted Groundcrew	855	0.82 (0.48,1.38)	0.446	0.72 (0.28,1.81)	0.483

Table 16-6. Analysis of WBC Count (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

		Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]				
			Number (%)		Abnormal Low vs. Normal		Abnormal High vs. Normal		
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]		p-Value
Low	139	13 (9.4)	125 (89.9)	1 (0.7)	1.03 (0.79,1.33)	0.834	1.01 (0.50,2.04)		0.972
Medium	143	12 (8.4)	128 (89.5)	3 (2.1)					
High	137	12 (8.8)	124 (90.5)	1 (0.7)					

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)				
	Abnormal Low vs. Normal			Abnormal High vs. Normal	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value		Adjusted Relative Risk (95% C.I.)[a]	p-Value
419	1.08 (0.82,1.43)	0.576		1.04 (0.49,2.21)	0.908

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with an abnormally high WBC count.

Table 16-6. Analysis of WBC Count (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Abnormal High vs. Normal Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	128 (10.9)	1,017 (86.8)	26 (2.2)				
Background RH	351	37 (10.5)	303 (86.3)	11 (3.1)	0.91 (0.61,1.34)	0.628	1.24 (0.60,2.55)	0.566
Low RH	210	17 (8.1)	191 (91.0)	2 (1.0)	0.72 (0.42,1.22)	0.216	0.42 (0.10,1.77)	0.237
High RH	209	20 (9.6)	186 (89.0)	3 (1.4)	0.91 (0.55,1.49)	0.696	0.72 (0.21,2.40)	0.587
Low plus High RH	419	37 (8.8)	377 (90.0)	5 (1.2)	0.80 (0.55,1.18)	0.271	0.55 (0.20,1.46)	0.228

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Abnormal Low vs. Normal Adjusted Relative Risk (95% C.I.)[a]	p-Value	Abnormal High vs. Normal Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168				
Background RH	350	0.89 (0.60,1.34)	0.578	1.34 (0.63,2.83)	0.443
Low RH	210	0.70 (0.41,1.22)	0.210	0.36 (0.08,1.53)	0.165
High RH	209	1.14 (0.67,1.94)	0.633	0.54 (0.16,1.83)	0.320
Low plus High RH	419	0.90 (0.60,1.34)	0.590	0.44 (0.16,1.18)	0.102

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-6. Analysis of WBC Count (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

| | | 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log$_2$ (1987 Dioxin)[a] | | | |
| | | | Number (%) | | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	27 (10.4)	225 (86.9)	7 (2.7)	0.95 (0.81,1.10)	0.469	0.65 (0.47,0.91)	0.011*
Medium	257	25 (9.7)	227 (88.3)	5 (1.9)				
High	254	22 (8.7)	228 (89.8)	4 (1.6)				

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (1987 Dioxin) | | | | |
| | Abnormal Low vs. Normal | | | Abnormal High vs. Normal | |
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value		Adjusted Relative Risk (95% C.I.)[a]	p-Value
769	1.05 (0.86,1.27)	0.655		0.61 (0.43,0.86)	0.005**

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with an abnormally high WBC count.

16.2.2.1.5 Hemoglobin (Continuous)

No significant results were found in the Model 1 through Model 4 unadjusted and adjusted analyses of hemoglobin in its continuous form (Table 16-7(a-h): p>0.16 for all contrasts).

Table 16-7. Analysis of Hemoglobin (gm/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*15.30*	*0.04 (-0.07,0.15)*	*0.505*
	Comparison	*1,171*	*15.26*		
Officer	Ranch Hand	306	15.13	0.01 (-0.17,0.19)	0.916
	Comparison	460	15.12		
Enlisted Flyer	Ranch Hand	133	15.28	-0.10 (-0.37,0.17)	0.483
	Comparison	185	15.38		
Enlisted Groundcrew	Ranch Hand	332	15.46	0.12 (-0.05,0.29)	0.164
	Comparison	526	15.34		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*15.01*	*0.02 (-0.09,0.12)*	*0.738*
	Comparison	*1,168*	*14.99*		
Officer	Ranch Hand	305	14.93	0.03 (-0.14,0.20)	0.767
	Comparison	460	14.91		
Enlisted Flyer	Ranch Hand	133	15.02	-0.13 (-0.39,0.14)	0.346
	Comparison	185	15.15		
Enlisted Groundcrew	Ranch Hand	332	15.02	0.07 (-0.10,0.23)	0.421
	Comparison	523	14.96		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	139	15.32	15.31	0.022	0.046 (0.044)	0.296
Medium	143	15.24	15.23			
High	137	15.46	15.48			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 16-7. Analysis of Hemoglobin (gm/dL) (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	139	15.20	0.114	-0.043 (0.049)	0.383
Medium	143	15.00			
High	137	15.13			

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,171	15.26	15.26		
Background RH	351	15.25	15.22	-0.04 (-0.19,0.11)	0.581
Low RH	210	15.32	15.33	0.07 (-0.11,0.25)	0.470
High RH	209	15.36	15.38	0.12 (-0.06,0.30)	0.188
Low plus High RH	419	15.34	15.36	0.09 (-0.04,0.23)	0.179

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,168	14.99		
Background RH	350	15.00	0.01 (-0.13,0.15)	0.895
Low RH	210	15.07	0.08 (-0.09,0.25)	0.355
High RH	209	14.92	-0.08 (-0.25,0.10)	0.404
Low plus High RH	419	15.00	0.00 (-0.13,0.14)	0.964

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-7. Analysis of Hemoglobin (gm/dL) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean**	**R^2**	**Slope (Standard Error)**	**p-Value**
Low	259	15.25	0.002	0.032 (0.028)	0.246
Medium	257	15.28			
High	254	15.37			

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	258	15.14	0.082	-0.020 (0.032)	0.519
Medium	257	15.17			
High	254	15.04			

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

16.2.2.1.6 Hemoglobin (Discrete)

No significant results were seen in the unadjusted or adjusted Model 1 hemoglobin analyses for the officer or the enlisted flyer stratum or for the overall contrast of Ranch Hands and Comparisons (Table 16-8(a,b): $p>0.15$ for all analyses). A significant difference in the percentage of participants with abnormally high hemoglobin levels was observed between Ranch Hand and Comparison in the enlisted groundcrew stratum (Table 16-8(a): $p=0.039$ for the unadjusted analysis). Nine Comparison groundcrew (1.7%) had abnormally high hemoglobin levels, and no Ranch Hand groundcrew participants had abnormally high hemoglobin levels. Adjusted analysis was not performed because of the lack of Ranch Hands with abnormally high hemoglobin levels.

No other association between categorized hemoglobin and dioxin levels in Model 2 through Model 4 unadjusted and adjusted analyses was significant (Table 16-8(c-h): $p>0.25$ for all analyses).

Table 16-8. Analysis of Hemoglobin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal Unadjusted Relative Risk (95% C.I.)	p-Value	Abnormal High vs. Normal Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*88 (11.4)*	*680 (88.2)*	*3 (0.4)*	*0.98 (0.74,1.31)*	*0.904*	*0.41 (0.11,1.48)*	0.173
	Comparison	*1,171*	*135 (11.5)*	*1,025 (87.5)*	*11 (0.9)*				
Officer	Ranch Hand	306	40 (13.1)	265 (86.6)	1 (0.3)	0.95 (0.62,1.45)	0.809	1.49 (0.11,20.89)	0.765
	Comparison	460	63 (13.7)	396 (86.1)	1 (0.2)				
Enlisted Flyer	Ranch Hand	133	17 (12.8)	114 (85.7)	2 (1.5)	1.30 (0.65,2.60)	0.467	2.89 (0.54,15.40)	0.213
	Comparison	185	19 (10.3)	165 (89.2)	1 (0.5)				
Enlisted Groundcrew	Ranch Hand	332	31 (9.3)	301 (90.7)	0 (0.0)	0.90 (0.57,1.44)	0.663	--	0.039*[a]
	Comparison	526	53 (10.1)	464 (88.2)	9 (1.7)				

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with abnormally high hemoglobin.

--: Results were not presented because of the sparse number of participants with abnormally high hemoglobin.

 *: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Abnormal Low vs. Normal Adjusted Relative Risk (95% C.I.)	p-Value	Abnormal High vs. Normal Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,938*	*1.00 (0.75,1.34)*	*0.989*	*0.39 (0.11,1.41)*	*0.151*
Officer	765	0.93 (0.60,1.43)	0.731	1.46 (0.10,20.48)	0.778
Enlisted Flyer	318	1.34 (0.66,2.72)	0.415	2.63 (0.48,14.32)	0.264
Enlisted Groundcrew	855	0.97 (0.60,1.56)	0.898	--	--

--: Results were not presented because of the sparse number of participants with abnormally high hemoglobin.

Note: Results were not adjusted for race because of the sparse number of participants with abnormally high hemoglobin.

Table 16-8. Analysis of Hemoglobin (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)[a]				
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]	p-Value
Low	139	13 (9.4)	125 (89.9)	1 (0.7)	0.97 (0.77,1.22)	0.788	0.41 (0.04,4.64)	0.472
Medium	143	20 (14.0)	123 (86.0)	0 (0.0)				
High	137	14 (10.2)	123 (89.8)	0 (0.0)				

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)				
	Abnormal Low vs. Normal			Abnormal High vs. Normal	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value		Adjusted Relative Risk (95% C.I.)[a]	p-Value
419	1.10 (0.86,1.40)	0.448		0.42 (0.03,6.68)	0.542

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, and current cigarette smoking because of the sparse number of Ranch Hands with abnormally high hemoglobin.

Table 16-8. Analysis of Hemoglobin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	**n**	**Abnormal Low**	**Normal**	**Abnormal High**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Comparison	1,171	135 (11.5)	1,025 (87.5)	11 (0.9)				
Background RH	351	41 (11.7)	308 (87.7)	2 (0.6)	1.11 (0.76,1.62)	0.584	0.69 (0.15,3.16)	0.632
Low RH	210	21 (10.0)	188 (89.5)	1 (0.5)	0.82 (0.50,1.34)	0.424	0.47 (0.06,3.67)	0.470
High RH	209	26 (12.4)	183 (87.6)	0 (0.0)	0.99 (0.63,1.56)	0.963	--	0.329[c]
Low plus High RH	419	47 (11.2)	371 (88.5)	1 (0.2)	0.90 (0.63,1.29)	0.564	--	0.272[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with abnormally high hemoglobin.
--: Results were not presented because of the sparse number of participants with abnormally high hemoglobin.

Note: RH = Ranch Hand.   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	**n**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Comparison	1,168				
Background RH	350	1.01 (0.68,1.50)	0.964	0.86 (0.17,4.24)	0.854
Low RH	210	0.81 (0.49,1.34)	0.406	0.53 (0.07,4.23)	0.552
High RH	209	1.33 (0.82,2.16)	0.254	--	--
Low plus High RH	419	1.04 (0.71,1.50)	0.856	--	--

[a]Relative risk and confidence interval relative to Comparisons.
--: Results were not presented because of the sparse number of participants with abnormally high hemoglobin.

Note: RH = Ranch Hand.   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

   Results were not adjusted for race because of the sparse number of participants with abnormally high hemoglobin.

Table 16-8. Analysis of Hemoglobin (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

| 1987 Dioxin Category Summary Statistics | | | | | Analysis Results for Log$_2$ (1987 Dioxin)[a] | | | |
| | | | | | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
			Number (%)					
Low	259	29 (11.2)	229 (88.4)	1 (0.4)	0.99 (0.86,1.14)	0.924	0.79 (0.38,1.64)	0.523
Medium	257	28 (10.9)	227 (88.3)	2 (0.8)				
High	254	31 (12.2)	223 (87.8)	0 (0.0)				

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (1987 Dioxin) | | | | |
| | Abnormal Low vs. Normal | | Abnormal High vs. Normal | | |
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
769	1.03 (0.88,1.21)	0.687	0.64 (0.25,1.67)	0.365

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race, military occupation, and current cigarette smoking because of the sparse number of Ranch Hands with abnormally high hemoglobin.

16.2.2.1.7 Hematocrit (Continuous)

No significant relations were detected between hematocrit in its continuous form and dioxin or exposure group for Model 1 through Model 4 unadjusted and adjusted analyses (Table 16-9(a-h): p>0.17 for all analyses).

Table 16-9. Analysis of Hematocrit (percent) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*45.83*	*0.13 (-0.22,0.49)*	*0.459*
	Comparison	*1,171*	*45.70*		
Officer	Ranch Hand	306	45.21	0.02 (-0.54,0.58)	0.940
	Comparison	460	45.19		
Enlisted Flyer	Ranch Hand	133	45.92	-0.18 (-1.05,0.68)	0.681
	Comparison	185	46.10		
Enlisted Groundcrew	Ranch Hand	332	46.37	0.37 (-0.16,0.90)	0.175
	Comparison	526	46.00		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*45.28*	*0.06 (-0.28,0.41)*	*0.719*
	Comparison	*1,168*	*45.22*		
Officer	Ranch Hand	305	44.89	0.05 (-0.50,0.60)	0.857
	Comparison	460	44.84		
Enlisted Flyer	Ranch Hand	133	45.39	-0.30 (-1.14,0.55)	0.489
	Comparison	185	45.69		
Enlisted Groundcrew	Ranch Hand	332	45.43	0.21 (-0.31,0.73)	0.425
	Comparison	523	45.22		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	139	45.88	45.84	0.016	0.094 (0.139)	0.497
Medium	143	45.72	45.70			
High	137	46.18	46.24			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 16-9. Analysis of Hematocrit (percent) (Continuous) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	139	45.67	0.098	-0.180 (0.156)	0.250
Medium	143	45.17			
High	137	45.33			

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,171	45.70	45.70		
Background RH	351	45.71	45.61	-0.09 (-0.56,0.38)	0.702
Low RH	210	45.91	45.94	0.23 (-0.34,0.81)	0.421
High RH	209	45.94	46.03	0.33 (-0.25,0.90)	0.262
Low plus High RH	419	45.92	45.99	0.28 (-0.15,0.72)	0.205

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,168	45.22		
Background RH	350	45.30	0.08 (-0.38,0.54)	0.721
Low RH	210	45.45	0.23 (-0.33,0.79)	0.417
High RH	209	44.94	-0.28 (-0.86,0.29)	0.332
Low plus High RH	419	45.19	-0.03 (-0.45,0.40)	0.904

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-9. Analysis of Hematocrit (percent) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean**	**R^2**	**Slope (Standard Error)**	**p-Value**
Low	259	45.71	0.001	0.072 (0.089)	0.415
Medium	257	45.75			
High	254	46.01			

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	258	45.86	0.067	-0.108 (0.102)	0.290
Medium	257	45.84			
High	254	45.40			

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

16.2.2.1.8 Hematocrit (Discrete)

No significant associations were found in Model 1, Model 2, or Model 4 unadjusted and adjusted analyses of hematocrit in its discrete form (Table 16-10(a-d,g,h): p>0.08 for all analyses).

A significant inverse relation was seen in the Model 3 unadjusted and adjusted analyses of abnormally low hematocrit when comparing Ranch Hands in the low dioxin category to the Comparison group (Table 16-10(e,f): Unadjusted RR=0.35, p=0.044; Adjusted RR=0.34, p=0.043). Abnormally low hematocrit was found in 5.1 percent of the Comparisons and 1.9 percent of the Ranch Hands in the low dioxin category. No other unadjusted or adjusted Model 3 contrast was significant (Table 16-10(e,f): p>0.09 for all analyses).

Table 16-10. Analysis of Hematocrit (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
			Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)	p-Value	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*34 (4.4)*	*731 (94.8)*	*6 (0.8)*	*0.85 (0.55,1.31)*	*0.471*	*0.90 (0.33,2.50)*	*0.845*
	Comparison	*1,171*	*60 (5.1)*	*1,101 (94.0)*	*10 (0.9)*				
Officer	Ranch Hand	306	18 (5.9)	286 (93.5)	2 (0.7)	0.93 (0.51,1.71)	0.823	3.01 (0.27,33.32)	0.370
	Comparison	460	29 (6.3)	430 (93.5)	1 (0.2)				
Enlisted Flyer	Ranch Hand	133	5 (3.8)	126 (94.7)	2 (1.5)	0.87 (0.28,2.72)	0.808	1.39 (0.19,9.99)	0.744
	Comparison	185	8 (4.3)	175 (94.6)	2 (1.1)				
Enlisted Groundcrew	Ranch Hand	332	11 (3.3)	319 (96.1)	2 (0.6)	0.74 (0.36,1.55)	0.428	0.44 (0.09,2.15)	0.313
	Comparison	526	23 (4.4)	496 (94.3)	7 (1.3)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Adjusted Relative Risk (95% C.I.)	p-Value	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,938*	*0.88 (0.57,1.36)*	*0.561*	*0.83 (0.30,2.34)*	*0.731*
Officer	765	0.95 (0.52,1.76)	0.880	2.93 (0.26,32.53)	0.381
Enlisted Flyer	318	0.90 (0.28,2.82)	0.850	1.23 (0.17,8.94)	0.836
Enlisted Groundcrew	855	0.78 (0.37,1.63)	0.507	0.40 (0.08,2.00)	0.264

Note: Results were not adjusted for race because of the sparse number of participants with abnormally high hematocrit.

Table 16-10. Analysis of Hematocrit (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

		Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)[a]				
			Number (%)		Abnormal Low vs. Normal		Abnormal High vs. Normal		
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	
Low	139	1 (0.7)	137 (98.6)	1 (0.7)	1.23 (0.86,1.75)	0.264	1.48 (0.69,3.18)	0.319	
Medium	143	7 (4.9)	136 (95.1)	0 (0.0)					
High	137	7 (5.1)	128 (93.4)	2 (1.5)					

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)				
	Abnormal Low vs. Normal		Abnormal High vs. Normal		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value	
419	1.38 (0.95,2.00)	0.089	1.51 (0.70,3.25)	0.290	

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, and current cigarette smoking because of the sparse number of Ranch Hands with abnormally high hematocrit.

Table 16-10. Analysis of Hematocrit (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

| Dioxin Category | n | Number (%) | | | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
		Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	60 (5.1)	1,101 (94.0)	10 (0.9)				
Background RH	351	19 (5.4)	329 (93.7)	3 (0.9)	1.13 (0.66,1.94)	0.646	1.13 (0.30,4.16)	0.859
Low RH	210	4 (1.9)	205 (97.6)	1 (0.5)	0.35 (0.13,0.97)	0.044*	0.51 (0.06,4.02)	0.522
High RH	209	11 (5.3)	196 (93.8)	2 (1.0)	0.97 (0.50,1.88)	0.926	1.01 (0.22,4.69)	0.991
Low plus High RH	419	15 (3.6)	401 (95.7)	3 (0.7)	0.58 (0.31,1.10)	0.096	0.72 (0.18,2.80)	0.632

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-10. Analysis of Hematocrit (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

		Abnormal Low vs. Normal		Abnormal High vs. Normal	
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168				
Background RH	350	1.03 (0.59,1.78)	0.925	1.23 (0.31,4.87)	0.765
Low RH	210	0.34 (0.12,0.97)	0.043*	0.54 (0.07,4.28)	0.558
High RH	209	1.37 (0.67,2.79)	0.382	0.71 (0.15,3.42)	0.668
Low plus High RH	419	0.69 (0.36,1.32)	0.260	0.62 (0.16,2.43)	0.491

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race because of the sparse number of participants with abnormally high hematocrit.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

		1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	13 (5.0)	244 (94.2)	2 (0.8)	0.94 (0.76,1.17)	0.584	1.14 (0.70,1.86)	0.593
Medium	257	9 (3.5)	246 (95.7)	2 (0.8)				
High	254	12 (4.7)	240 (94.5)	2 (0.8)				

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

Table 16-10. Analysis of Hematocrit (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)				
	Abnormal Low vs. Normal		Abnormal High vs. Normal		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
769	1.02 (0.77,1.37)	0.867	1.12 (0.61,2.07)	0.705

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with abnormally high hematocrit.

16.2.2.1.9 Platelet Count (Continuous)

The difference in mean platelet count between all Ranch Hands and Comparisons in the Model 1 unadjusted and adjusted analyses was not significant, and no significant difference was seen between Ranch Hands and Comparisons in the officer or enlisted groundcrew strata (Table 16-11(a,b): p>0.06 for all analyses). A significant difference in mean platelet counts was seen, however, between Ranch Hands and Comparisons within the enlisted flyer stratum (Table 16-11(a,b): difference of means = 18.2 thousand/mm^3, p=0.006; difference of adjusted means = 18.4 thousand/mm^3, p=0.005).

The Model 2 unadjusted analysis of platelet count in its continuous form revealed a significant association with initial dioxin (Table 16-11(c): Slope=0.148, p=0.024). After adjustment for covariates, the association was no longer significant (Table 16-11(d): p=0.881).

Unadjusted Model 3 analyses showed that mean platelet counts were significantly greater for Ranch Hands in the high dioxin category and Ranch Hands in the low and high dioxin categories combined than for Comparisons (Table 16-11(e): difference of means = 13.7 thousand/mm^3 for the high dioxin category, p=0.002; difference of means = 6.9 thousand/mm^3 for the low and high dioxin categories combined, p=0.038). After adjusting for the covariates, however, the mean platelet counts were no longer significantly different between Comparisons and Ranch Hands in the high category or in the low and high dioxin categories combined (Table 16-11(f): p>0.05 for both analyses). No other contrasts of Ranch Hands and Comparisons in Model 3 were significant (Table 16-11(e,f): p>0.60 for all remaining contrasts).

The unadjusted and adjusted analyses of Model 4 showed no significant association between platelet count and 1987 dioxin levels (Table 16-11(g,h): p>0.12 for both analyses).

16.2.2.1.10   Platelet Count (Discrete)

No significant associations between exposure group or dioxin levels and the categorized form of platelet count were observed in the unadjusted and adjusted analyses for Model 1 through Model 4 (Table 16-12(a-h): p>0.09 for all analyses).

Table 16-11. Analysis of Platelet Count (thousand/mm^3) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*770*	*237.6*	*3.2*	*0.247*
	Comparison	*1,168*	*234.4*		
Officer	Ranch Hand	305	223.7	-7.5	0.077
	Comparison	460	231.2		
Enlisted Flyer	Ranch Hand	133	244.3	18.2	0.006**
	Comparison	184	226.1		
Enlisted Groundcrew	Ranch Hand	332	247.9	7.7	0.064
	Comparison	524	240.2		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

**: Statistically significant (p-value≤0.010).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*769*	*240.9*	*3.3*	*0.224*
	Comparison	*1,165*	*237.6*		
Officer	Ranch Hand	304	230.4	-7.4	0.079
	Comparison	460	237.8		
Enlisted Flyer	Ranch Hand	133	249.5	18.4	0.005**
	Comparison	184	231.1		
Enlisted Groundcrew	Ranch Hand	332	247.9	7.4	0.072
	Comparison	521	240.5		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

**: Statistically significant (p-value≤0.010).

Table 16-11. Analysis of Platelet Count (thousand/mm³) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	139	227.2	226.6	0.033	0.148 (0.065)	0.024*
Medium	143	247.2	246.9			
High	137	244.6	245.6			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of platelet count versus log_2 (initial dioxin).

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	234.6	0.108	0.011 (0.074)	0.881
Medium	143	245.1			
High	137	241.6			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of platelet count versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,168	234.4	234.6		
Background RH	350	234.9	232.1	-2.5	0.494
Low RH	210	233.9	234.8	0.2	0.954
High RH	209	245.5	248.3	13.7	0.002**
Low plus High RH	419	239.6	241.5	6.9	0.038*

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,165	238.0		
Background RH	349	237.9	-0.1	0.982
Low RH	210	240.2	2.2	0.604
High RH	209	246.8	8.8	0.051
Low plus High RH	419	243.5	5.5	0.099

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-11. Analysis of Platelet Count (thousand/mm³) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	259	235.4	0.003	0.063 (0.042)	0.129
Medium	256	231.5			
High	254	245.8			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of platelet count versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	258	240.6	0.087	0.004 (0.048)	0.932
Medium	256	237.9			
High	254	242.9			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of platelet count versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 16-12. Analysis of Platelet Count (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
			Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)	p-Value	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*12 (1.6)*	*753 (97.8)*	*5 (0.6)*	*0.82 (0.40,1.67)*	*0.583*	*0.54 (0.19,1.50)*	*0.234*
	Comparison	*1,168*	*22 (1.9)*	*1,132 (96.9)*	*14 (1.2)*				
Officer	Ranch Hand	305	9 (3.0)	295 (96.7)	1 (0.3)	2.30 (0.81,6.52)	0.118	0.77 (0.07,8.48)	0.828
	Comparison	460	6 (1.3)	452 (98.3)	2 (0.4)				
Enlisted Flyer	Ranch Hand	133	1 (0.8)	131 (98.5)	1 (0.8)	0.27 (0.03,2.35)	0.237	1.36 (0.08,21.92)	0.829
	Comparison	184	5 (2.7)	178 (96.7)	1 (0.5)				
Enlisted Groundcrew	Ranch Hand	332	2 (0.6)	327 (98.5)	3 (0.9)	0.28 (0.06,1.27)	0.098	0.42 (0.12,1.51)	0.184
	Comparison	524	11 (2.1)	502 (95.8)	11 (2.1)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Adjusted Relative Risk (95% C.I.)	p-Value	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,934*	*0.81 (0.40,1.65)*	*0.559*	*0.53 (0.19,1.50)*	*0.231*
Officer	764	2.29 (0.81,6.52)	0.119	0.77 (0.07,8.58)	0.835
Enlisted Flyer	317	0.27 (0.03,2.32)	0.232	1.23 (0.08,20.09)	0.883
Enlisted Groundcrew	853	0.27 (0.06,1.24)	0.093	0.41 (0.11,1.49)	0.175

Table 16-12. Analysis of Platelet Count (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]	p-Value
		Initial Dioxin Category Summary Statistics Number (%)			**Analysis Results for Log$_2$ (Initial Dioxin)[a]** Abnormal Low vs. Normal		Abnormal High vs. Normal	
Low	139	3 (2.2)	136 (97.8)	0 (0.0)	0.66 (0.30,1.44)	0.299	1.19 (0.44,3.22)	0.726
Medium	143	1 (0.7)	140 (97.9)	2 (1.4)				
High	137	1 (0.7)	136 (99.3)	0 (0.0)				

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
	Analysis Results for Log$_2$ (Initial Dioxin) Abnormal Low vs. Normal		Abnormal High vs. Normal	
419	0.73 (0.32,1.64)	0.441	1.08 (0.32,3.61)	0.897

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with an abnormally high platelet count.

Table 16-12. Analysis of Platelet Count (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Abnormal High vs. Normal Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,168	22 (1.9)	1,132 (96.9)	14 (1.2)				
Background RH	350	7 (2.0)	340 (97.1)	3 (0.9)	1.22 (0.51,2.91)	0.654	0.65 (0.19,2.31)	0.509
Low RH	210	3 (1.4)	207 (98.6)	0 (0.0)	0.70 (0.21,2.37)	0.567	--	0.220[c]
High RH	209	2 (1.0)	205 (98.1)	2 (1.0)	0.44 (0.10,1.89)	0.269	0.85 (0.19,3.80)	0.834
Low plus High RH	419	5 (1.2)	412 (98.3)	2 (0.5)	0.55 (0.20,1.51)	0.247	--	0.320[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormally high platelet count.
--: Results were not presented because of the sparse number of participants with an abnormally high platelet count.

Note: RH = Ranch Hand.   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Abnormal Low vs. Normal Adjusted Relative Risk (95% C.I.)[a]	p-Value	Abnormal High vs. Normal Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,165				
Background RH	349	1.18 (0.48,2.86)	0.719	0.83 (0.23,3.02)	0.777
Low RH	210	0.73 (0.21,2.51)	0.616	--	--
High RH	209	0.42 (0.09,1.89)	0.258	0.56 (0.12,2.61)	0.463
Low plus High RH	419	0.55 (0.20,1.53)	0.254	--	--

[a]Relative risk and confidence interval relative to Comparisons.
--: Results were not presented because of the sparse number of participants with an abnormally high platelet count.

Note: RH = Ranch Hand.   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-12. Analysis of Platelet Count (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

| | | 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log$_2$ (1987 Dioxin)[a] | | | |
| | | | Number (%) | | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	4 (1.5)	252 (97.3)	3 (1.2)	0.80 (0.55,1.16)	0.244	0.63 (0.36,1.12)	0.113
Medium	256	6 (2.3)	250 (97.7)	0 (0.0)				
High	254	2 (0.8)	250 (98.4)	2 (0.8)				

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (1987 Dioxin) | | | | |
| | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	0.91 (0.55,1.51)	0.722	0.67 (0.37,1.22)	0.191

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with an abnormally high platelet count.

16.2.2.1.11 RBC Morphology

The percentage of participants with an abnormal RBC morphology was not significantly different between Ranch Hands and Comparisons in the officer or enlisted flyer strata, nor in the overall comparison of Ranch Hands and Comparisons in the Model 1 unadjusted and adjusted analyses (Table 16-13(a,b): p>0.13 for all analyses). The percentage of Ranch Hands with abnormal RBC morphology was significantly greater than Comparisons in the enlisted groundcrew stratum in both the Model 1 unadjusted and adjusted analyses (Table 16-13(a,b): Unadjusted RR=1.88, p=0.044; Adjusted RR=2.10, p=0.022). Among Ranch Hand enlisted groundcrew, 6.9 percent had an abnormal RBC morphology, while 3.8 percent of Comparison groundcrew had abnormal RBC morphology.

No significant associations between RBC morphology and either initial or 1987 dioxin levels in the unadjusted and adjusted analyses of Model 2 and Model 4 were observed (Table 16-13(c,d,g,h): p>0.47 for all analyses).

The Model 3 unadjusted analysis revealed no significant differences in abnormal RBC morphology between Ranch Hands and Comparisons (Table 16-13(e): p>0.05 for all contrasts). After adjustment for covariates, significant differences were noted between Comparisons and Ranch Hands in the high category and Ranch Hands in the low and high dioxin categories combined (Table 16-13(f): Adjusted RR=1.93 for Ranch Hands in the high category, p=0.047; Adjusted RR=1.74 for Ranch Hands in the low and high dioxin categories combined, p=0.021). Fewer Comparisons (5.2%) had an abnormal RBC morphology than Ranch Hands in the high dioxin category (6.7%) or the low and high dioxin categories combined (7.6%). No difference was seen between Ranch Hands in the background or low categories and Comparisons in the adjusted Model 3 analyses (Table 16-13(f): p>0.12 for both analyses).

Table 16-13. Analysis of RBC Morphology

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Abnormal**	**Unadjusted Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*771*	*51 (6.6)*	*1.29 (0.88,1.89)*	*0.197*
	Comparison	*1,171*	*61 (5.2)*		
Officer	Ranch Hand	306	18 (5.9)	0.86 (0.47,1.58)	0.635
	Comparison	460	31 (6.7)		
Enlisted Flyer	Ranch Hand	133	10 (7.5)	1.42 (0.57,3.52)	0.446
	Comparison	185	10 (5.4)		
Enlisted Groundcrew	Ranch Hand	332	23 (6.9)	1.88 (1.02,3.49)	0.044*
	Comparison	526	20 (3.8)		

*: Statistically significant (0.010<p-value≤0.050).

Table 16-13. Analysis of RBC Morphology (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,938*	*1.36 (0.92,2.01)*	*0.131*
Officer	765	0.87 (0.47,1.60)	0.658
Enlisted Flyer	318	1.55 (0.61,3.97)	0.359
Enlisted Groundcrew	855	2.10 (1.12,3.97)	0.022*

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	10 (7.2)	0.95 (0.71,1.25)	0.689
Medium	143	14 (9.8)		
High	137	8 (5.8)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
419	1.13 (0.81,1.59)	0.476

[a]Relative risk for a twofold increase in initial dioxin.

Table 16-13. Analysis of RBC Morphology (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	61 (5.2)		
Background RH	351	19 (5.4)	1.05 (0.62,1.80)	0.846
Low RH	210	18 (8.6)	1.70 (0.98,2.94)	0.058
High RH	209	14 (6.7)	1.29 (0.71,2.36)	0.405
Low plus High RH	419	32 (7.6)	1.48 (0.95,2.32)	0.084

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	350	1.02 (0.59,1.76)	0.951
Low RH	210	1.57 (0.89,2.77)	0.123
High RH	209	1.93 (1.01,3.70)	0.047*
Low plus High RH	419	1.74 (1.09,2.78)	0.021*

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	15 (5.8)	1.02 (0.86,1.22)	0.800
Medium	257	15 (5.8)		
High	254	21 (8.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 16-13. Analysis of RBC Morphology (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
769	1.06 (0.85,1.32)	0.597

[a]Relative risk for a twofold increase in 1987 dioxin.

16.2.2.1.12 Absolute Neutrophils (Segs)

No significant associations between segmented neutrophils and either exposure groups or dioxin levels were observed in Model 1 through Model 4 unadjusted and adjusted analyses (Table 16-14(a-h): p>0.06 for all analyses).

Table 16-14. Analysis of Absolute Neutrophils (segs) (thousand/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*771*	*3.68*	*0.07*	*0.213*
	Comparison	*1,171*	*3.61*		
Officer	Ranch Hand	306	3.50	0.05	0.598
	Comparison	460	3.45		
Enlisted Flyer	Ranch Hand	133	3.82	0.14	0.324
	Comparison	185	3.67		
Enlisted Groundcrew	Ranch Hand	332	3.80	0.07	0.411
	Comparison	526	3.73		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*770*	*3.42*	*0.04*	*0.497*
	Comparison	*1,168*	*3.38*		
Officer	Ranch Hand	305	3.29	0.04	0.649
	Comparison	460	3.25		
Enlisted Flyer	Ranch Hand	133	3.45	0.08	0.528
	Comparison	185	3.36		
Enlisted Groundcrew	Ranch Hand	332	3.53	0.02	0.839
	Comparison	523	3.51		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	139	3.68	3.69	0.005	0.001 (0.012)	0.925
Medium	143	3.94	3.94			
High	137	3.65	3.63			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of absolute neutrophils (segs) versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	3.45	0.142	-0.013 (0.013)	0.337
Medium	143	3.54			
High	137	3.27			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of absolute neutrophils (segs) versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 16-14. Analysis of Absolute Neutrophils (segs) (thousand/mm^3) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,171	3.61	3.61		
Background RH	351	3.59	3.61	0.00	0.980
Low RH	210	3.77	3.77	0.16	0.094
High RH	209	3.74	3.72	0.11	0.247
Low plus High RH	419	3.75	3.74	0.13	0.062

[a]Transformed from square root scale.

[b]Adjusted for body mass index at the time of the blood measurement of dioxin.

[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[d]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,168	3.37		
Background RH	350	3.40	0.03	0.694
Low RH	210	3.50	0.13	0.153
High RH	209	3.34	-0.03	0.702
Low plus High RH	419	3.42	0.05	0.499

[a]Transformed from square root scale.

[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-14. Analysis of Absolute Neutrophils (segs) (thousand/mm³) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log₂ (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R²**	**Slope (Standard Error)[b]**	**p-Value**
Low	259	3.61	0.001	0.008 (0.007)	0.302
Medium	257	3.63			
High	254	3.80			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of absolute neutrophils (segs) versus log₂ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log₂ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R²**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	258	3.47	0.120	-0.008 (0.008)	0.364
Medium	257	3.40			
High	254	3.43			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of absolute neutrophils (segs) versus log₂ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

16.2.2.1.13 Absolute Neutrophils (Bands) (Nonzero Measurements)

For participants who had neutrophilic bands present, the unadjusted and adjusted analyses of Model 1 through Model 4 revealed no significant associations between absolute neutrophilic bands and either exposure group or dioxin levels (Table 16-15(a-h): p>0.11 for all analyses).

Table 16-15. Analysis of Absolute Neutrophils (bands) (thousand/mm^3) (Nonzero Measurements)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*626*	*0.174*	*0.007*	*0.350*
	Comparison	*932*	*0.168*		
Officer	Ranch Hand	254	0.169	0.004	0.720
	Comparison	368	0.165		
Enlisted Flyer	Ranch Hand	109	0.190	0.029	0.123
	Comparison	144	0.162		
Enlisted Groundcrew	Ranch Hand	263	0.174	0.001	0.895
	Comparison	420	0.172		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented
 because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*625*	*0.150*	*0.003*	*0.665*
	Comparison	*931*	*0.148*		
Officer	Ranch Hand	253	0.147	0.002	0.799
	Comparison	368	0.144		
Enlisted Flyer	Ranch Hand	109	0.158	0.019	0.225
	Comparison	144	0.139		
Enlisted Groundcrew	Ranch Hand	263	0.152	-0.003	0.736
	Comparison	419	0.156		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented
 because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log₂ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	109	0.189	0.189	0.001	-0.022 (0.035)	0.539
Medium	114	0.198	0.198			
High	111	0.163	0.163			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus log₂ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	109	0.154	0.074	-0.064 (0.040)	0.111
Medium	114	0.146			
High	111	0.114			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus log₂ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	932	0.168	0.168		
Background RH	291	0.165	0.166	-0.002	0.885
Low RH	163	0.187	0.186	0.018	0.137
High RH	171	0.179	0.178	0.010	0.390
Low plus High RH	334	0.183	0.182	0.014	0.124

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-15. *Analysis of Absolute Neutrophils (bands) (thousand/mm^3) (Nonzero Measurements) (Continued)*

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	931	0.147		
Background RH	290	0.144	-0.003	0.722
Low RH	163	0.159	0.012	0.272
High RH	171	0.151	0.004	0.699
Low plus High RH	334	0.155	0.008	0.331

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	217	0.160	0.002	0.021 (0.021)	0.310
Medium	203	0.186			
High	205	0.180			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	216	0.133	0.037	0.012 (0.025)	0.613
Medium	203	0.152			
High	205	0.146			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute neutrophils (bands) versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

16.2.2.1.14 Absolute Neutrophils (Bands) (Zero versus Nonzero)

The percentage of participants with no neutrophilic bands present was not significantly different among exposure or dioxin groups in the Model 1 through Model 4 unadjusted and adjusted analyses (Table 16-16(a-h): p≥0.15 for analyses).

Table 16-16. Analysis of Absolute Neutrophils (bands) (Zero vs. Nonzero)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Zero	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*145 (18.8)*	*0.90 (0.72,1.14)*	*0.384*
	Comparison	*1,171*	*239 (20.4)*		
Officer	Ranch Hand	306	52 (17.0)	0.82 (0.56,1.19)	0.297
	Comparison	460	92 (20.0)		
Enlisted Flyer	Ranch Hand	133	24 (18.0)	0.77 (0.44,1.36)	0.370
	Comparison	185	41 (22.2)		
Enlisted Groundcrew	Ranch Hand	332	69 (20.8)	1.04 (0.74,1.46)	0.823
	Comparison	526	106 (20.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,938*	*0.92 (0.73,1.16)*	*0.471*
Officer	765	0.82 (0.56,1.20)	0.310
Enlisted Flyer	318	0.79 (0.45,1.38)	0.401
Enlisted Groundcrew	855	1.07 (0.76,1.51)	0.698

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Zero	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	30 (21.6)	0.96 (0.80,1.16)	0.681
Medium	143	29 (20.3)		
High	137	26 (19.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 16-16. Analysis of Absolute Neutrophils (bands) (Zero vs. Nonzero) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
419	0.99 (0.80,1.24)	0.963

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Zero	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	239 (20.4)		
Background RH	351	60 (17.1)	0.79 (0.58,1.09)	0.150
Low RH	210	47 (22.4)	1.13 (0.79,1.61)	0.505
High RH	209	38 (18.2)	0.88 (0.60,1.28)	0.496
Low plus High RH	419	85 (20.3)	0.99 (0.75,1.31)	0.969

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	350	0.82 (0.59,1.13)	0.221
Low RH	210	1.15 (0.80,1.64)	0.456
High RH	209	0.88 (0.59,1.31)	0.527
Low plus High RH	419	1.01 (0.76,1.34)	0.971

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Zero	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	42 (16.2)	1.04 (0.93,1.17)	0.463
Medium	257	54 (21.0)		
High	254	49 (19.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
769	1.05 (0.92,1.20)	0.496

[a]Relative risk for a twofold increase in 1987 dioxin.

16.2.2.1.15 Absolute Lymphocytes

No significant differences in mean absolute lymphocyte counts were seen between exposure groups in Model 1 unadjusted or adjusted analyses (Table 16-17(a,b): p>0.24 for all analyses) or between absolute lymphocyte counts and 1987 dioxin levels in Model 4 unadjusted and adjusted analyses (Table 16-17(g,h): p>0.09 for all analyses).

The unadjusted Model 2 analysis of absolute lymphocytes revealed a significant association between absolute lymphocytes and initial dioxin (Table 16-17(c): Slope=0.039, p=0.008). After adjustment for covariates, however, the association was not significant (Table 16-17(d): p=0.092).

In the unadjusted Model 3 analyses, a significant difference in absolute lymphocytes was seen between Comparisons and Ranch Hands in the high dioxin category (Table 16-17(e): difference of means = 0.12 thousand/mm^3, p=0.031). The association was no longer significant after adjustment for covariates (Table 16-17(f): p=0.592). No other significant associations were seen in the Model 3 unadjusted or adjusted analyses (Table 16-17(e,f): p>0.19 for all contrasts).

Table 16-17. Analysis of Absolute Lymphocytes (thousand/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*771*	*1.64*	*0.01*	*0.778*
	Comparison	*1,171*	*1.63*		
Officer	Ranch Hand	306	1.53	-0.01	0.845
	Comparison	460	1.54		
Enlisted Flyer	Ranch Hand	133	1.60	-0.05	0.481
	Comparison	185	1.65		
Enlisted Groundcrew	Ranch Hand	332	1.77	0.06	0.245
	Comparison	526	1.71		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*770*	*1.65*	*0.00*	*0.975*
	Comparison	*1,168*	*1.65*		
Officer	Ranch Hand	305	1.59	-0.01	0.825
	Comparison	460	1.60		
Enlisted Flyer	Ranch Hand	133	1.60	-0.06	0.401
	Comparison	185	1.67		
Enlisted Groundcrew	Ranch Hand	332	1.73	0.04	0.438
	Comparison	523	1.69		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 16-17. Analysis of Absolute Lymphocytes (thousand/mm³) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log₂ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	139	1.55	1.55	0.017	0.039 (0.015)	0.008**
Medium	143	1.70	1.70			
High	137	1.74	1.74			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of absolute lymphocytes versus $\log_2$ (initial dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log₂ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	1.54	0.083	0.028 (0.017)	0.092
Medium	143	1.64			
High	137	1.68			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute lymphocytes versus $\log_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,171	1.63	1.63		
Background RH	351	1.61	1.61	-0.02	0.635
Low RH	210	1.58	1.58	-0.05	0.316
High RH	209	1.75	1.75	0.12	0.031*
Low plus High RH	419	1.66	1.66	0.03	0.448

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,168	1.65		
Background RH	350	1.66	0.01	0.798
Low RH	210	1.59	-0.06	0.195
High RH	209	1.68	0.03	0.592
Low plus High RH	419	1.63	-0.02	0.626

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-17. Analysis of Absolute Lymphocytes (thousand/mm³) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	259	1.58	0.004	0.016 (0.010)	0.099
Medium	257	1.61			
High	254	1.74			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute lymphocytes versus $\log_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	258	1.60	0.056	-0.007 (0.011)	0.521
Medium	257	1.60			
High	254	1.61			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute lymphocytes versus $\log_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

16.2.2.1.16 Absolute Monocytes

No significant associations were seen between absolute monocyte counts and either exposure groups or dioxin levels in Model 1 through Model 4 unadjusted and adjusted analyses (Table 16-18(a-h): p>0.17 for all analyses).

Table 16-18. Analysis of Absolute Monocytes (thousand/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*771*	*0.423*	*0.007*	*0.487*
	Comparison	*1,171*	*0.416*		
Officer	Ranch Hand	306	0.408	0.004	0.807
	Comparison	460	0.404		
Enlisted Flyer	Ranch Hand	133	0.429	0.025	0.311
	Comparison	185	0.404		
Enlisted Groundcrew	Ranch Hand	332	0.434	0.004	0.803
	Comparison	526	0.430		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*770*	*0.414*	*0.004*	*0.691*
	Comparison	*1,168*	*0.410*		
Officer	Ranch Hand	305	0.410	0.003	0.835
	Comparison	460	0.407		
Enlisted Flyer	Ranch Hand	133	0.411	0.019	0.412
	Comparison	185	0.392		
Enlisted Groundcrew	Ranch Hand	332	0.427	-0.002	0.919
	Comparison	523	0.428		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Table 16-18. Analysis of Absolute Monocytes (thousand/mm³) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	139	0.403	0.403	0.004	0.007 (0.006)	0.234
Medium	143	0.435	0.435			
High	137	0.421	0.420			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of absolute monocytes versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	0.377	0.098	0.009 (0.007)	0.174
Medium	143	0.407			
High	137	0.403			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of absolute monocytes versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,171	0.416	0.416		
Background RH	351	0.426	0.428	0.012	0.351
Low RH	210	0.418	0.417	0.001	0.922
High RH	209	0.421	0.419	0.003	0.819
Low plus High RH	419	0.420	0.418	0.002	0.829

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-18. Analysis of Absolute Monocytes (thousand/mm³) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,168	0.411		
Background RH	350	0.426	0.015	0.250
Low RH	210	0.403	-0.008	0.607
High RH	209	0.403	-0.008	0.632
Low plus High RH	419	0.403	-0.008	0.511

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	259	0.433	<0.001	0.002 (0.004)	0.602
Medium	257	0.405			
High	254	0.430			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of absolute monocytes versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	258	0.437	0.041	-0.003 (0.004)	0.457
Medium	257	0.392			
High	254	0.402			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of absolute monocytes versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

16.2.2.1.17 Absolute Eosinophils (Nonzero Measurements)

For participants with eosinophils present, all unadjusted and adjusted analyses in Models 1 through 4 were not significant (Table 16-19(a–h): p>0.12 for all analyses).

Table 16-19. Analysis of Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*699*	*0.161*	*0.006*	*0.318*
	Comparison	*1,045*	*0.155*		
Officer	Ranch Hand	281	0.147	-0.003	0.706
	Comparison	410	0.150		
Enlisted Flyer	Ranch Hand	120	0.180	0.018	0.221
	Comparison	169	0.162		
Enlisted Groundcrew	Ranch Hand	298	0.167	0.010	0.257
	Comparison	466	0.158		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*698*	*0.156*	*0.005*	*0.394*
	Comparison	*1,042*	*0.151*		
Officer	Ranch Hand	280	0.144	-0.003	0.710
	Comparison	410	0.147		
Enlisted Flyer	Ranch Hand	120	0.168	0.016	0.249
	Comparison	169	0.153		
Enlisted Groundcrew	Ranch Hand	298	0.160	0.008	0.350
	Comparison	463	0.152		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

	Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	124	0.160	0.160	<0.001	-0.004 (0.028)	0.882
Medium	127	0.171	0.171			
High	127	0.153	0.153			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of absolute eosinophils versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Initial Dioxin Category Summary Statistics		Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	124	0.160	0.029	-0.021 (0.032)	0.526
Medium	127	0.161			
High	127	0.145			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute eosinophils versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,045	0.155	0.155		
Background RH	320	0.160	0.161	0.006	0.429
Low RH	185	0.167	0.167	0.012	0.202
High RH	193	0.155	0.155	0.000	0.940
Low plus High RH	378	0.161	0.161	0.006	0.436

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-19. Analysis of Absolute Eosinophils (thousand/mm³) (Nonzero Measurements) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,042	0.151		
Background RH	319	0.160	0.009	0.227
Low RH	185	0.158	0.007	0.402
High RH	193	0.144	-0.007	0.427
Low plus High RH	378	0.151	0.000	0.999

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	236	0.161	<0.001	0.002 (0.017)	0.911
Medium	231	0.160			
High	231	0.162			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute eosinophils versus $\log_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	235	0.164	0.039	-0.031 (0.020)	0.121
Medium	231	0.153			
High	231	0.143			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute eosinophils versus $\log_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

16.2.2.1.18 Absolute Eosinophils (Zero versus Nonzero)

The percentage of participants with eosinophils present was not significantly associated with exposure group or dioxin in any of the Model 1 through 4 unadjusted and adjusted analyses (Table 16-20(a–h): p>0.12 for all analyses).

Table 16-20. Analysis of Absolute Eosinophils (Zero vs. Nonzero)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Zero	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*72 (9.3)*	*0.85 (0.63,1.16)*	*0.309*
	Comparison	*1,171*	*126 (10.8)*		
Officer	Ranch Hand	306	25 (8.2)	0.73 (0.44,1.21)	0.220
	Comparison	460	50 (10.9)		
Enlisted Flyer	Ranch Hand	133	13 (9.8)	1.14 (0.53,2.47)	0.731
	Comparison	185	16 (8.6)		
Enlisted Groundcrew	Ranch Hand	332	34 (10.2)	0.89 (0.57,1.38)	0.595
	Comparison	526	60 (11.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,938*	*0.86 (0.63,1.17)*	*0.340*
Officer	765	0.73 (0.44,1.20)	0.212
Enlisted Flyer	318	1.15 (0.53,2.48)	0.728
Enlisted Groundcrew	855	0.90 (0.58,1.41)	0.650

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Zero	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	15 (10.8)	0.96 (0.75,1.23)	0.768
Medium	143	16 (11.2)		
High	137	10 (7.3)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
419	0.99 (0.74,1.32)	0.955

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Zero	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	126 (10.8)		
Background RH	351	31 (8.8)	0.82 (0.54,1.24)	0.341
Low RH	210	25 (11.9)	1.12 (0.71,1.76)	0.639
High RH	209	16 (7.7)	0.68 (0.39,1.17)	0.160
Low plus High RH	419	41 (9.8)	0.87 (0.60,1.27)	0.470

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	350	0.85 (0.56,1.30)	0.463
Low RH	210	1.13 (0.71,1.79)	0.605
High RH	209	0.65 (0.37,1.13)	0.126
Low plus High RH	419	0.86 (0.58,1.26)	0.425

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Zero**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	259	23 (8.9)	0.97 (0.84,1.13)	0.739
Medium	257	26 (10.1)		
High	254	23 (9.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
769	0.93 (0.78,1.12)	0.447

[a]Relative risk for a twofold increase in 1987 dioxin.

16.2.2.1.19 Absolute Basophils (Nonzero Measurements)

For participants who had basophils, no significant relations were observed between the absolute basophil count and exposure group or initial dioxin in Model 1 or Model 2 unadjusted and adjusted analyses (Table 16-21(a–d): p≥0.06 for all analyses). In Model 3 unadjusted analyses, the mean absolute basophil count was significantly greater for Comparisons than Ranch Hands in the background category (Table 16-21(e): difference of means = -0.006 thousand/mm^3, p=0.030). This result was no longer significant after adjusting for covariates (Table 16-21(f): p=0.051). No other Model 3 unadjusted or adjusted result was significant (Table 16-21(e,f): p>0.50 for all analyses).

In the unadjusted analysis of Model 4, a significant positive relation between absolute basophil count and 1987 dioxin levels was observed (Table 16-21(g): Slope=0.035, p=0.012). This result was no longer significant after adjustment for covariates (Table 16-21(h): p=0.235).

Table 16-21. Analysis of Absolute Basophils (thousand/mm^3) (Nonzero Measurements)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*397*	*0.074*	*-0.003*	*0.102*
	Comparison	*620*	*0.078*		
Officer	Ranch Hand	164	0.070	-0.006	0.060
	Comparison	237	0.076		
Enlisted Flyer	Ranch Hand	75	0.075	-0.004	0.476
	Comparison	101	0.079		
Enlisted Groundcrew	Ranch Hand	158	0.078	-0.000	0.927
	Comparison	282	0.079		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*397*	*0.071*	*-0.004*	*0.087*
	Comparison	*617*	*0.075*		
Officer	Ranch Hand	164	0.068	-0.006	0.061
	Comparison	237	0.074		
Enlisted Flyer	Ranch Hand	75	0.072	-0.003	0.541
	Comparison	101	0.075		
Enlisted Groundcrew	Ranch Hand	158	0.074	-0.001	0.689
	Comparison	279	0.076		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 16-21. Analysis of Absolute Basophils (thousand/mm³) (Nonzero Measurements) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	72	0.069	0.069	0.004	0.021 (0.023)	0.370
Medium	70	0.084	0.084			
High	74	0.077	0.077			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of absolute basophils versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	72	0.067	0.048	-0.010 (0.027)	0.708
Medium	70	0.078			
High	74	0.069			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute basophils versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	620	0.078	0.078		
Background RH	181	0.071	0.072	-0.006	0.030*
Low RH	108	0.076	0.076	-0.002	0.610
High RH	108	0.077	0.077	-0.001	0.859
Low plus High RH	216	0.077	0.076	-0.002	0.650

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	617	0.075		
Background RH	181	0.070	-0.005	0.051
Low RH	108	0.073	-0.002	0.520
High RH	108	0.073	-0.002	0.502
Low plus High RH	216	0.073	-0.002	0.384

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	137	0.068	0.016	0.035 (0.014)	0.012*
Medium	131	0.077			
High	129	0.079			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute basophils versus log$_2$ (1987 dioxin).

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	137	0.066	0.046	0.020 (0.017)	0.235
Medium	131	0.073			
High	129	0.073			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute basophils versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

16.2.2.1.20 Absolute Basophils (Zero versus Nonzero)

No associations between the percentage of participants with basophils present and either exposure group or dioxin levels were seen in Model 1 through Model 4 unadjusted and adjusted analyses (Table 16-22(a-h): p>0.08 for all analyses).

Table 16-22. Analysis of Absolute Basophils (Zero vs. Nonzero)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Zero		Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*374*	*(48.5)*	*1.06 (0.88,1.27)*	*0.530*
	Comparison	*1,171*	*551*	*(47.1)*		
Officer	Ranch Hand	306	142	(46.4)	0.92 (0.69,1.23)	0.574
	Comparison	460	223	(48.5)		
Enlisted Flyer	Ranch Hand	133	58	(43.6)	0.93 (0.59,1.46)	0.751
	Comparison	185	84	(45.4)		
Enlisted Groundcrew	Ranch Hand	332	174	(52.4)	1.27 (0.97,1.68)	0.086
	Comparison	526	244	(46.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,938*	*1.06 (0.88,1.27)*	*0.521*
Officer	765	0.91 (0.68,1.22)	0.546
Enlisted Flyer	318	0.94 (0.60,1.47)	0.774
Enlisted Groundcrew	855	1.27 (0.97,1.68)	0.086

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Zero	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	67 (48.2)	0.99 (0.86,1.15)	0.928
Medium	143	73 (51.0)		
High	137	63 (46.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
419	0.99 (0.84,1.18)	0.939

[a]Relative risk for a twofold increase in initial dioxin.

Table 16-22. Analysis of Absolute Basophils (Zero vs. Nonzero) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Zero	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	551 (47.1)		
Background RH	351	170 (48.4)	1.04 (0.81,1.32)	0.773
Low RH	210	102 (48.6)	1.07 (0.80,1.43)	0.660
High RH	209	101 (48.3)	1.07 (0.80,1.44)	0.648
Low plus High RH	419	203 (48.4)	1.07 (0.86,1.34)	0.555

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	350	1.04 (0.81,1.32)	0.776
Low RH	210	1.08 (0.80,1.45)	0.627
High RH	209	1.06 (0.78,1.44)	0.694
Low plus High RH	419	1.07 (0.85,1.34)	0.561

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Zero	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	122 (47.1)	0.98 (0.90,1.08)	0.729
Medium	257	126 (49.0)		
High	254	125 (49.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 16-22. Analysis of Absolute Basophils (Zero vs. Nonzero) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
769	0.95 (0.85,1.05)	0.300

[a]Relative risk for a twofold increase in 1987 dioxin.

16.2.2.1.21 Fibrinogen (Continuous)

No significant differences were seen between fibrinogen and exposure group in Model 1 unadjusted and adjusted analyses (Table 16-23(a,b): p>0.20 for all analyses) or between fibrinogen and initial dioxin in Model 2 unadjusted and adjusted analyses (Table 16-23(c,d): p>0.48 for each analyses).

In Model 3 unadjusted analyses, the mean fibrinogen was significantly higher for Ranch Hands in the low dioxin category than for Comparisons (Table 16-23(e): difference of means = 11.3 mg/dL, p=0.017). After adjustment for covariates, the difference was no longer significant (Table 16-23(f): p=0.119). No other contrasts in Model 3 unadjusted and adjusted analyses were significant (Table 16-23(e,f): p>0.06 for all other analyses).

Fibrinogen levels were significantly associated with 1987 dioxin levels in Model 4 unadjusted analysis (Table 16-23(g): Slope=0.009, p=0.021), but were not significantly associated after adjusting for covariates (Table 16-23(h): p=0.411).

Table 16-23. Analysis of Fibrinogen (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*770*	*357.0*	*3.0*	*0.300*
	Comparison	*1,171*	*353.9*		
Officer	Ranch Hand	305	350.9	5.7	0.207
	Comparison	460	345.2		
Enlisted Flyer	Ranch Hand	133	361.5	-5.5	0.450
	Comparison	185	367.1		
Enlisted Groundcrew	Ranch Hand	332	360.8	3.6	0.417
	Comparison	526	357.1		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 16-23. Analysis of Fibrinogen (mg/dL) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*769*	*363.6*	*2.1*	*0.471*
	Comparison	*1,168*	*361.5*		
Officer	Ranch Hand	304	354.6	5.1	0.252
	Comparison	460	349.5		
Enlisted Flyer	Ranch Hand	133	360.8	-7.6	0.279
	Comparison	185	368.4		
Enlisted Groundcrew	Ranch Hand	332	372.3	3.0	0.504
	Comparison	523	369.4		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	139	357.8	358.6	0.025	-0.001 (0.007)	0.840
Medium	143	370.7	371.1			
High	137	357.4	356.2			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of fibrinogen versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	350.9	0.146	-0.005 (0.007)	0.485
Medium	143	359.5			
High	137	346.4			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of fibrinogen versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 16-23. Analysis of Fibrinogen (mg/dL) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,171	353.9	353.8		
Background RH	350	350.9	353.2	-0.6	0.872
Low RH	210	365.9	365.1	11.3	0.017*
High RH	209	358.1	355.8	2.0	0.674
Low plus High RH	419	362.0	360.4	6.6	0.064

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented
  because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant $(0.010 < \text{p-value} \leq 0.050)$.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,168	361.0		
Background RH	349	362.1	1.1	0.771
Low RH	210	368.3	7.3	0.119
High RH	209	360.7	-0.3	0.948
Low plus High RH	419	364.5	3.5	0.329

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented
  because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-23. Analysis of Fibrinogen (mg/dL) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	258	347.3	0.007	0.009 (0.004)	0.021*
Medium	257	360.9			
High	254	362.8			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of fibrinogen versus log_2 (1987 dioxin).

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	257	354.4	0.124	0.004 (0.005)	0.411
Medium	257	359.5			
High	254	361.3			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of fibrinogen versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

16.2.2.1.22 *Fibrinogen (Discrete)*

No significant associations were observed between fibrinogen in its discrete form and either exposure group or dioxin levels in unadjusted and adjusted Model 1 through Model 4 analyses (Table 16-24(a-h): p>0.21 for all analyses).

Table 16-24. Analysis of Fibrinogen (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*49 (6.4)*	*1.22 (0.83,1.79)*	*0.324*
	Comparison	*1,171*	*62 (5.3)*		
Officer	Ranch Hand	305	16 (5.2)	1.54 (0.76,3.12)	0.235
	Comparison	460	16 (3.5)		
Enlisted Flyer	Ranch Hand	133	12 (9.0)	1.05 (0.48,2.29)	0.908
	Comparison	185	16 (8.6)		
Enlisted Groundcrew	Ranch Hand	332	21 (6.3)	1.12 (0.63,1.98)	0.708
	Comparison	526	30 (5.7)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,937*	*1.19 (0.80,1.76)*	*0.396*
Officer	764	1.55 (0.76,3.17)	0.228
Enlisted Flyer	318	0.98 (0.44,2.18)	0.968
Enlisted Groundcrew	855	1.10 (0.61,1.97)	0.755

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	5 (3.6)	1.05 (0.79,1.39)	0.741
Medium	143	14 (9.8)		
High	137	9 (6.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
419	1.03 (0.75,1.42)	0.862

[a]Relative risk for a twofold increase in initial dioxin.

Table 16-24. Analysis of Fibrinogen (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	62 (5.3)		
Background RH	350	21 (6.0)	1.25 (0.75,2.09)	0.395
Low RH	210	16 (7.6)	1.43 (0.81,2.54)	0.219
High RH	209	12 (5.7)	1.00 (0.53,1.91)	0.991
Low plus High RH	419	28 (6.7)	1.20 (0.75,1.91)	0.445

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	349	1.37 (0.81,2.34)	0.243
Low RH	210	1.28 (0.71,2.31)	0.402
High RH	209	0.94 (0.48,1.82)	0.851
Low plus High RH	419	1.10 (0.68,1.77)	0.700

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	258	15 (5.8)	1.03 (0.86,1.24)	0.710
Medium	257	14 (5.4)		
High	254	20 (7.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 16-24. Analysis of Fibrinogen (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (1987 Dioxin) | |
| | Adjusted Relative Risk | |
n	(95% C.I.)[a]	p-Value
768	0.98 (0.79,1.22)	0.855

[a]Relative risk for a twofold increase in 1987 dioxin.

16.2.2.1.23 ESR (Continuous)

No significant associations were seen between ESR and exposure group in Model 1 unadjusted and adjusted analyses (Table 16-25(a,b): p>0.10 for all analyses) or initial dioxin in Model 2 unadjusted and adjusted analyses (Table 16-25(c,d): p>0.53 for both analyses).

Ranch Hands in the low dioxin category and Ranch Hands in the low and high dioxin categories combined had significantly higher ESRs than Comparisons in the unadjusted Model 3 analyses (Table 16-25(e): difference of means = 1.33 mm/hour for the low dioxin category, p=0.018; difference of means = 1.02 mm/hour for the low and high dioxin categories combined, p=0.015). After adjusting for covariates, the results were significant for the low and high dioxin categories combined (Table 16-25(f): difference of adjusted means = 0.99 mm/hour, p=0.027), but were not significant for the low dioxin category (Table 16-25(f): p=0.060). The adjusted mean ESR was 7.81 mm/hour for Comparisons compared to 8.02 mm/hour for Ranch Hands in the background dioxin category, 8.92 mm/hour for Ranch Hands in the low dioxin category, 8.69 mm/hour for Ranch Hands in the high dioxin category, and 8.80 mm/hour for Ranch Hands in the low and high dioxin categories combined.

The relation between ESR and 1987 dioxin levels was significant in the unadjusted analysis of Model 4 (Table 16-25(g): Slope=0.060, p=0.005), but not significant when adjusted for covariates (Table 16-25(h): p=0.086).

Table 16-25. Analysis of ESR (mm/hour) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*771*	*7.76*	*0.51*	*0.131*
	Comparison	*1,171*	*7.25*		
Officer	Ranch Hand	306	7.35	0.71	0.156
	Comparison	460	6.65		
Enlisted Flyer	Ranch Hand	133	8.46	0.20	0.827
	Comparison	185	8.26		
Enlisted Groundcrew	Ranch Hand	332	7.87	0.40	0.439
	Comparison	526	7.47		

[a]Transformed from natural logarithm scale of ESR + 0.1.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of ESR + 0.1.
[c]P-value was based on difference of means on natural logarithm scale of ESR + 0.1.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*770*	*8.42*	*0.57*	*0.109*
	Comparison	*1,168*	*7.86*		
Officer	Ranch Hand	305	7.41	0.65	0.186
	Comparison	460	6.76		
Enlisted Flyer	Ranch Hand	133	8.54	0.25	0.777
	Comparison	185	8.29		
Enlisted Groundcrew	Ranch Hand	332	9.32	0.59	0.321
	Comparison	523	8.73		

[a]Transformed from natural logarithm scale of ESR + 0.1.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of ESR + 0.1.
[c]P-value was based on difference of means on natural logarithm scale of ESR + 0.1.

Table 16-25. Analysis of ESR (mm/hour) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	139	7.63	7.73	0.031	-0.004 (0.033)	0.904
Medium	143	10.10	10.16			
High	137	7.91	7.75			

[a]Transformed from natural logarithm scale of ESR + 0.1.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of ESR + 0.1 versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	6.85	0.102	0.023 (0.038)	0.537
Medium	143	9.26			
High	137	7.68			

[a]Transformed from natural logarithm scale of ESR + 0.1.
[b]Slope and standard error based on natural logarithm of ESR + 0.1 versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,171	7.25	7.23		
Background RH	351	6.96	7.26	0.03	0.939
Low RH	210	8.68	8.56	1.33	0.018*
High RH	209	8.31	7.96	0.73	0.181
Low plus High RH	419	8.50	8.25	1.02	0.015*

[a]Transformed from natural logarithm scale of ESR + 0.1.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of ESR + 0.1.
[d]P-value was based on difference of means on natural logarithm scale of ESR + 0.1.

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-25. Analysis of ESR (mm/hour) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,168	7.81		
Background RH	350	8.02	0.21	0.650
Low RH	210	8.92	1.11	0.060
High RH	209	8.69	0.88	0.143
Low plus High RH	419	8.80	0.99	0.027*

[a]Transformed from natural logarithm scale of ESR + 0.1.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of ESR + 0.1.
[c]P-value was based on difference of means on natural logarithm scale of ESR + 0.1.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	259	6.67	0.010	0.060 (0.021)	0.005**
Medium	257	8.06			
High	254	8.70			

[a]Transformed from natural logarithm scale of ESR + 0.1.
[b]Slope and standard error based on natural logarithm of ESR + 0.1 versus log_2 (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

Table 16-25. Analysis of ESR (mm/hour) (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	258	6.85	0.095	0.042 (0.024)	0.086
Medium	257	7.43			
High	254	8.32			

[a]Transformed from natural logarithm scale of ESR + 0.1.
[b]Slope and standard error based on natural logarithm of ESR + 0.1 versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

16.2.2.1.24   ESR (Discrete)

ESR in the discrete form was not significantly associated with exposure group or dioxin levels in Model 1 through Model 4 unadjusted and adjusted analyses (Table 16-26(a-h): p>0.19 for all analyses).

Table 16-26. Analysis of ESR (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*771*	*90 (11.7)*	*1.19 (0.89,1.59)*	*0.242*
	Comparison	*1,171*	*117 (10.0)*		
Officer	Ranch Hand	306	31 (10.1)	1.33 (0.80,2.20)	0.270
	Comparison	460	36 (7.8)		
Enlisted Flyer	Ranch Hand	133	20 (15.0)	1.38 (0.72,2.67)	0.335
	Comparison	185	21 (11.4)		
Enlisted Groundcrew	Ranch Hand	332	39 (11.7)	1.03 (0.67,1.59)	0.879
	Comparison	526	60 (11.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,938*	*1.22 (0.91,1.65)*	*0.191*
Officer	765	1.37 (0.82,2.29)	0.230
Enlisted Flyer	318	1.40 (0.71,2.76)	0.325
Enlisted Groundcrew	855	1.06 (0.68,1.66)	0.796

Table 16-26. Analysis of ESR (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	13 (9.4)	0.99 (0.80,1.23)	0.934
Medium	143	24 (16.8)		
High	137	17 (12.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
419	1.09 (0.84,1.40)	0.531

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,171	117 (10.0)		
Background RH	351	36 (10.3)	1.17 (0.78,1.74)	0.444
Low RH	210	28 (13.3)	1.33 (0.85,2.09)	0.206
High RH	209	26 (12.4)	1.15 (0.72,1.82)	0.560
Low plus High RH	419	54 (12.9)	1.24 (0.87,1.75)	0.232

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 16-26. Analysis of ESR (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,168		
Background RH	350	1.30 (0.86,1.98)	0.216
Low RH	210	1.25 (0.78,1.98)	0.352
High RH	209	1.20 (0.74,1.95)	0.457
Low plus High RH	419	1.22 (0.85,1.76)	0.275

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	23 (8.9)	1.09 (0.95,1.24)	0.239
Medium	257	34 (13.2)		
High	254	33 (13.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
769	1.04 (0.87,1.23)	0.679

[a]Relative risk for a twofold increase in 1987 dioxin.

16.3 DISCUSSION

The hematologic dependent variables studied were automated blood cell counts and standardized measurements of hemoglobin concentration, hematocrit, plasma fibrinogen, and ESR obtained from peripheral venous blood samples of AFHS participants. Identification of specific WBC types (e.g., segmented neutrophils, band neutrophils, lymphocytes, monocytes, eosinophils, basophils) was confirmed by visual inspection by trained hematology laboratory technicians of peripheral blood smears stained with Wright-Giemsa reagents.

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The observed significant associations between the hematologic dependent variables and the covariates of age, race, and body mass index were all in accordance with known effects that age, genetics, and obesity have on erythrocytes, leukocytes, and platelets. Similarly, all of the significant hematologic dependent variable-covariate associations with cigarette smoking were expected, based on the known hematologic pathophysiology of smokers. Fibrinogen levels, leukocyte counts, and ESRs rise as inflammation increases. As expected and as seen in this study, inflammation increases as age, cigarette smoking, and obesity increase. With the exceptions of segmented neutrophil number, fibrinogen level, and ESR, officers had hematologic differences from enlisted personnel that would be expected due to age because officers were, on average, older than enlisted personnel. Although older, officers had lower fibrinogen levels and ESRs, indicating that they may be healthier than enlisted personnel.

The differences noted between the Ranch Hand and Comparison participants reveal clues, but not answers, to potential hematologic problems among the Ranch Hands. These clues differ in what they point to, depending on the specific hematologic parameter being measured. The statistically significant increase in the number of RBC morphologic abnormalities noted among Ranch Hand enlisted groundcrew relative to Comparison enlisted groundcrew does not constitute evidence for a defined hematologic disorder. It does, however, provide a clue that future hematologic problems, such as hemolysis or myelodysplasia, may emerge in the Ranch Hand enlisted groundcrew.

The statistically significant increase in the mean ESR among Ranch Hands in the low and high dioxin categories combined does not constitute evidence for a defined hematologic disorder. As in the case of RBC morphologic abnormalities, however, it provides a clue that future problems, such as inflammatory disorders or monoclonal gammopathies, may emerge among Ranch Hands.

The finding of a statistically significant increase in mean platelet count among Ranch Hand enlisted flyers relative to Comparison enlisted flyers also does not indicate a definite hematologic disease. Elevated platelet counts can be associated with an inflammatory process, gastrointestinal hemorrhage, or myeloproliferative disorders.

The statistically significant relation between a lower WBC count and higher 1987 dioxin levels in Ranch Hands suggests that there may be a dose-response connection. Disorders such as myelodysplasia and aplastic anemia are associated with a decrease in WBCs. Leukemia, which is also associated with a decrease in WBCs, was analyzed in Chapter 10, Neoplasia Assessment.

In conclusion, the significant hematologic differences noted between the Ranch Hands and Comparisons may point to the possibility of a future emergence of hematologic problems, but they do not point to a specific diagnosis. Hemolysis, myelodysplasia, myeloproliferation, marrow aplasia, and leukemia would be among the disorders that could occur in the future. The increase in ESR for Ranch Hands, an increase that was also associated with increased smoking and increased obesity, also does not point to a specific diagnosis. Based on the results seen at this follow-up examination, careful observation for the development of inflammatory disorders and monoclonal gammopathies should be the focus of any future study of possible hematologic disorders on Ranch Hands.

16.4 SUMMARY

The hematology assessment was based only on laboratory data. Associations with herbicide exposure (i.e., group – Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable in the hematology assessment. The significant adjusted results are discussed in the sections below.

16.4.1   Model 1: Group Analysis

As shown in Table 16-27, the analysis of the continuous form of platelet count demonstrated a significant difference between Ranch Hands and Comparisons in the enlisted flyer stratum. The mean platelet count was higher for Ranch Hand enlisted flyers than for Comparison enlisted flyers. The only other significant difference between Ranch Hands and Comparisons in Model 1 analyses was in the enlisted groundcrew stratum for RBC morphology. Ranch Hand enlisted groundcrew were more likely to have an abnormal RBC morphology than Comparison enlisted groundcrew.

Table 16-27. Summary of Group Analysis (Model 1) for Hematology Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
Red Blood Cell (RBC) Count (C)	NS	ns	ns	NS
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS	NS	ns	ns
Abnormal High vs. Normal	ns	NS	ns	ns
White Blood Cell (WBC) Count (C)	NS	NS	NS	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	ns	ns	NS	ns
Abnormal High vs. Normal	ns	ns	NS	ns
Hemoglobin (C)	NS	NS	ns	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	ns	ns	NS	ns
Abnormal High vs. Normal	ns	NS	NS	p=0.039 (*)
Hematocrit (C)	NS	NS	ns	NS
Hematocrit (D)				
Abnormal Low vs. Normal	ns	ns	ns	ns
Abnormal High vs. Normal	ns	NS	NS	ns
Platelet Count (C)	NS	ns	p=0.006 (18.2)	NS
Platelet Count (D)				
Abnormal Low vs. Normal	ns	NS	ns	ns
Abnormal High vs. Normal	ns	ns	NS	ns
RBC Morphology (D)	NS	ns	NS	p=0.044 (1.88)
Absolute Neutrophils (Segs) (C)	NS	NS	NS	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS	NS	NS
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	ns	ns	NS
Absolute Lymphocytes (C)	NS	ns	ns	NS
Absolute Monocytes (C)	NS	NS	NS	NS
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns	NS	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	ns	NS	ns
Absolute Basophils (Nonzero Measurements) (C)	ns	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	NS	ns	ns	NS
Fibrinogen (C)	NS	NS	ns	NS
Fibrinogen (D)	NS	NS	NS	NS
ESR (C)	NS	NS	NS	NS
ESR (D)	NS	NS	NS	NS

--: The analysis was not performed because of the sparse number of participants with an abnormality.

*: Relative risk was not able to be calculated. Zero Ranch Hands and nine Comparisons had abnormally high hemoglobin.

Note: NS or ns: Not significant (p>0.05).
       C: Continuous form of dependent variable.
       D: Discrete form of dependent variable.

       The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

       A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

	ADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Laboratory				
Red Blood Cell (RBC) Count (C)	NS	ns	ns	NS
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS	NS	ns	ns
Abnormal High vs. Normal	ns	NS	ns	ns
White Blood Cell (WBC) Count (C)	NS	NS	NS	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	ns	ns	NS	ns
Abnormal High vs. Normal	ns	ns	NS	ns
Hemoglobin (C)	NS	NS	ns	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	ns	NS	NS	--
Hematocrit (C)	NS	NS	ns	NS
Hematocrit (D)				
Abnormal Low vs. Normal	ns	ns	ns	ns
Abnormal High vs. Normal	ns	NS	NS	ns
Platelet Count (C)	NS	ns	p=0.005 (18.4)	NS
Platelet Count (D)				
Abnormal Low vs. Normal	ns	NS	ns	ns
Abnormal High vs. Normal	ns	ns	NS	ns
RBC Morphology (D)	NS	ns	NS	p=0.022 (2.10)
Absolute Neutrophils (Segs) (C)	NS	NS	NS	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS	NS	ns
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	ns	ns	NS
Absolute Lymphocytes (C)	NS	ns	ns	NS
Absolute Monocytes (C)	NS	NS	NS	ns
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns	NS	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	ns	NS	ns

| | ADJUSTED | | | |
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Absolute Basophils (Nonzero Measurements) (C)	ns	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	NS	ns	ns	NS
Fibrinogen (C)	NS	NS	ns	NS
Fibrinogen (D)	NS	NS	ns	NS
ESR (C)	NS	NS	NS	NS
ESR (D)	NS	NS	NS	NS

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
   C: Continuous form of dependent variable.
   D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

16.4.2   Model 2: Initial Dioxin Analysis

No significant relations were seen between initial dioxin and any of the hematology variables after adjustment for covariates in Model 2 analyses. Table 16-28 shows the results of the initial dioxin analysis.

Table 16-28. **Summary of Initial Dioxin Analysis (Model 2) for Hematology Variables (Ranch Hands Only)**

Variable	Unadjusted	Adjusted
Laboratory		
Red Blood Cell (RBC) Count (C)	NS	ns
Red Blood Cell (RBC) Count (D)		
Abnormal Low vs. Normal	ns	NS
Abnormal High vs. Normal	NS	NS
White Blood Cell (WBC) Count (C)	NS	ns
White Blood Cell (WBC) Count (D)		
Abnormal Low vs. Normal	NS	NS
Abnormal High vs. Normal	NS	NS
Hemoglobin (C)	NS	ns
Hemoglobin (D)		
Abnormal Low vs. Normal	ns	NS
Abnormal High vs. Normal	ns	ns

Variable	Unadjusted	Adjusted
Hematocrit (C)	NS	ns
Hematocrit (D)		
Abnormal Low vs. Normal	NS	NS
Abnormal High vs. Normal	NS	NS
Platelet Count (C)	p=0.024 (0.148)	NS
Platelet Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	NS	NS
RBC Morphology (D)	ns	NS
Absolute Neutrophils (Segs) (C)	NS	ns
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	ns	ns
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	ns
Absolute Lymphocytes (C)	p=0.008 (0.039)	NS
Absolute Monocytes (C)	NS	NS
Absolute Eosinophils (Nonzero Measurements) (C)	ns	ns
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	NS	ns
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns
Fibrinogen (C)	ns	ns
Fibrinogen (D)	NS	NS
ESR (C)	ns	NS
ESR (D)	ns	NS

Note: NS or ns: Not significant (p>0.05).

       C: Continuous form of dependent variable.

       D: Discrete form of dependent variable.

       The p-value was given if p≤0.05. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

       A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

16.4.3 Model 3: Categorized Dioxin Analysis

A significant difference in abnormally low hematocrit levels was seen between Comparisons and Ranch Hands in the low dioxin category in the Model 3 analyses. Comparisons were significantly more likely to have abnormally low hematocrit levels than Ranch Hands in the low dioxin category. In addition, Ranch Hands in the high dioxin category and in the low and high dioxin categories combined had a significantly higher percentage of abnormal RBC morphology results than did Comparisons. Ranch Hands in the low and high dioxin categories combined also had a significantly higher mean ESR than Comparisons. Table 16-29 presents the results of the categorized dioxin analysis.

Table 16-29. Summary of Categorized Dioxin Analysis (Model 3) for Hematology Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Laboratory				
Red Blood Cell (RBC) Count (C)	ns	NS	NS	NS
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS	ns	ns	ns
Abnormal High vs. Normal	ns	ns	ns	ns
White Blood Cell (WBC) Count (C)	NS	NS	NS	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	ns	ns	ns	ns
Abnormal High vs. Normal	NS	ns	ns	ns
Hemoglobin (C)	ns	NS	NS	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	ns	ns	ns
Abnormal High vs. Normal	ns	ns	ns	ns
Hematocrit (C)	ns	NS	NS	NS
Hematocrit (D)				
Abnormal Low vs. Normal	NS	p=0.044 (0.35)	ns	ns
Abnormal High vs. Normal	NS	ns	NS	ns
Platelet Count (C)	ns	NS	p=0.002 (13.7)	p=0.038 (6.9)
Platelet Count (D)				
Abnormal Low vs. Normal	NS	ns	ns	ns
Abnormal High vs. Normal	ns	ns	ns	ns
RBC Morphology (D)	NS	NS	NS	NS
Absolute Neutrophils (Segs) (C)	NS	NS	NS	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	ns	NS	NS	NS
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	NS	ns	ns
Absolute Lymphocytes (C)	ns	ns	p=0.031 (0.12)	NS
Absolute Monocytes (C)	NS	NS	NS	NS
Absolute Eosinophils (Nonzero Measurements) (C)	NS	NS	NS	NS
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	NS	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	p=0.030 (-0.006)	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	NS	NS	NS	NS
Fibrinogen (C)	ns	p=0.017 (11.3)	NS	NS
Fibrinogen (D)	NS	NS	NS	NS
ESR (C)	NS	p=0.018 (1.33)	NS	p=0.015 (1.02)
ESR (D)	NS	NS	NS	NS

Note: NS or ns: Not significant (p>0.05).

       C: Continuous form of dependent variable.

       D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

	ADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Laboratory				
Red Blood Cell (RBC) Count (C)	NS	NS	ns	ns
Red Blood Cell (RBC) Count (D)				
Abnormal Low vs. Normal	NS	ns	NS	ns
Abnormal High vs. Normal	NS	ns	ns	ns
White Blood Cell (WBC) Count (C)	NS	NS	ns	NS
White Blood Cell (WBC) Count (D)				
Abnormal Low vs. Normal	ns	ns	NS	ns
Abnormal High vs. Normal	NS	ns	ns	ns
Hemoglobin (C)	NS	NS	ns	NS
Hemoglobin (D)				
Abnormal Low vs. Normal	NS	ns	NS	NS
Abnormal High vs. Normal	ns	ns	--	--
Hematocrit (C)	NS	NS	ns	ns
Hematocrit (D)				
Abnormal Low vs. Normal	NS	p=0.043 (0.34)	NS	ns
Abnormal High vs. Normal	NS	ns	ns	ns
Platelet Count (C)	ns	NS	NS	NS
Platelet Count (D)				
Abnormal Low vs. Normal	NS	ns	ns	ns
Abnormal High vs. Normal	ns	--	ns	--
RBC Morphology (D)	NS	NS	p=0.047 (1.93)	p=0.021 (1.74)
Absolute Neutrophils (Segs) (C)	NS	NS	ns	NS
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	ns	NS	NS	NS
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	ns	NS	ns	NS
Absolute Lymphocytes (C)	NS	ns	NS	ns
Absolute Monocytes (C)	NS	ns	ns	ns
Absolute Eosinophils (Nonzero Measurements) (C)	NS	NS	ns	NS

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	NS	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	ns	ns	ns	ns
Absolute Basophils (Zero vs. Nonzero) (D)	NS	NS	NS	NS
Fibrinogen (C)	NS	NS	ns	NS
Fibrinogen (D)	NS	NS	ns	NS
ESR (C)	NS	NS	NS	p=0.027 (0.99)
ESR (D)	NS	NS	NS	NS

--: The analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
     C: Continuous form of dependent variable.
     D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

16.4.4   Model 4: 1987 Dioxin Level Analysis

In the Model 4 analyses, only the WBC count varied significantly with 1987 dioxin levels. In analysis of both the continuous and discrete forms of WBC count, a significant inverse relation between WBC counts and 1987 dioxin levels was observed. Table 16-30 displays the results of the 1987 dioxin analysis.

Table 16-30. Summary of 1987 Dioxin Analysis (Model 4) for Hematology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Laboratory		
Red Blood Cell (RBC) Count (C)	NS	ns
Red Blood Cell (RBC) Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	NS	NS

Table 16-30. Summary of 1987 Dioxin Analysis (Model 4) for Hematology Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
White Blood Cell (WBC) Count (C)	NS	p=0.047 (-0.014)
White Blood Cell (WBC) Count (D)		
Abnormal Low vs. Normal	ns	NS
Abnormal High vs. Normal	p=0.011 (0.65)	p=0.005 (0.61)
Hemoglobin (C)	NS	ns
Hemoglobin (D)		
Abnormal Low vs. Normal	ns	NS
Abnormal High vs. Normal	ns	ns
Hematocrit (C)	NS	ns
Hematocrit (D)		
Abnormal Low vs. Normal	ns	NS
Abnormal High vs. Normal	NS	NS
Platelet Count (C)	NS	NS
Platelet Count (D)		
Abnormal Low vs. Normal	ns	ns
Abnormal High vs. Normal	ns	ns
RBC Morphology (D)	NS	NS
Absolute Neutrophils (Segs) (C)	NS	ns
Absolute Neutrophils (Bands) (Nonzero Measurements) (C)	NS	NS
Absolute Neutrophils (Bands) (Zero vs. Nonzero) (D)	NS	NS
Absolute Lymphocytes (C)	NS	ns
Absolute Monocytes (C)	NS	ns
Absolute Eosinophils (Nonzero Measurements) (C)	NS	ns
Absolute Eosinophils (Zero vs. Nonzero) (D)	ns	ns
Absolute Basophils (Nonzero Measurements) (C)	p=0.012 (0.035)	NS
Absolute Basophils (Zero vs. Nonzero) (D)	ns	ns
Fibrinogen (C)	p=0.021 (0.009)	NS
Fibrinogen (D)	NS	ns
ESR (C)	p=0.005 (0.060)	NS
ESR (D)	NS	NS

Note: NS or ns: Not significant (p>0.05).

     C: Continuous form of dependent variable.

     D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

16.4.5 Summary of Significant Results

Table 16-31 summarizes the significant results (p≤0.05) for the adjusted analyses that were performed for the hematology assessment. The dependent variable and its table reference are listed, along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and is explained in footnotes.

Table 16-31. Summary of Results from Significant Adjusted Analyses in the Hematology Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
WBC Count (16-5)	4	All RH: 1987 Dioxin	0.047	-0.014 (0.007)	Low: 5.98 thousand/mm^3 Medium: 5.81 thousand/mm^3 High: 5.83 thousand/mm^3	(a)
WBC Count (16-6)	4	All RH: 1987 Dioxin — Abnormal High vs. Normal	0.005	0.61 (0.43,0.86)	Low: 2.7% Medium: 1.9% High: 1.6%	(b)
Hematocrit (16-10)	3	Low RH vs. C: Abnormal Low vs. Normal	0.043	0.34 (0.12,0.97)	RH: 1.9% C: 5.1%	(c)
Platelet Count (16-11)	1	RH vs. C, Enlisted Flyer	0.005	18.4	RH: 249.5 thousand/mm^3 C: 231.1 thousand/mm^3	(d)
RBC Morphology (16-13)	1	RH vs. C, Enlisted Groundcrew	0.022	2.10 (1.12,3.97)	RH: 6.9% C: 3.8%	(e)
	3	High RH vs. C	0.047	1.93 (1.01,3.70)	RH: 6.7% C: 5.2%	(c)
	3	Low plus High RH vs. C	0.021	1.74 (1.09,2.78)	RH: 7.6% C: 5.2%	(c)
ESR (16-25)	3	Low plus High RH vs. C	0.027	0.99	RH: 8.80 mm/hour C: 7.81 mm/hour	(f)

(a): Continuous variable: slope and standard error were presented and were based on natural logarithm of dependent variable versus $\log_2$ (initial dioxin); adjusted means were presented for each of three 1987 dioxin categories.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(d): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each exposure group in contrast.

(e): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(f): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each dioxin category in contrast.

Note: RH = Ranch Hand.
          C = Comparison.

      Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
                       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
                       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

      Model 4:   Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

16.5 CONCLUSION

A few statistically significant findings were observed in the statistical analysis of the hematologic system. The mean platelet count was increased among Ranch Hand enlisted flyers. Ranch Hand enlisted groundcrew experienced an increased risk of abnormal RBC morphology. Ranch Hands in the low dioxin category had a decreased risk of abnormally low hematocrit levels. Ranch Hands in the high dioxin category and in the low and high dioxin categories combined had a significantly higher percentage of abnormal RBC morphology results. In addition, Ranch Hands in the low and high dioxin combined category had a higher mean ESR than did Comparisons. In analyses of both the continuous and discrete forms of WBC, a significant inverse relation between WBC counts and 1987 dioxin levels was observed.

The significant hematologic differences noted between the Ranch Hands and Comparisons may point to the possibility of a future emergence of hematologic problems, but they do not point to a specific diagnosis. Hemolysis, myelodysplasia, myeloproliferation, marrow aplasia, and leukemia would be among the disorders that could occur in the future. Hematologic malignancies are discussed in Chapter 10, Neoplasia Assessment.

The increase in ESR for Ranch Hands also does not point to a specific diagnosis. Based on the results seen at this follow-up examination, careful observation for the development of inflammatory disorders and monoclonal gammopathies should be the focus of any future study of possible hematologic disorders on Ranch Hands.

In conclusion, these data did not suggest an association between dioxin and any hematologic condition.

REFERENCES

1. Abadin, H.G., H.E. Murray, and J.S. Wheeler. 1998. The use of hematological effects in the development of minimal risk levels. *Regulatory Toxicology and Pharmacology* 28:61-6.

2. McConnell, E.E., J.A. Moore, and D.W. Dalgard. 1978. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rhesus monkeys (Macaca mulatta) following a single oral dose. *Toxicology and Applied Pharmacology* 43:175-87.

3. Kociba, R.J., P.A. Keeler, C.N. Park, and P.J. Gehring. 1976. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD): Results of a 13-week oral toxicity study in rats. *Toxicology and Applied Pharmacology* 35:553-74.

4. Weissberg, J.B., and J.G. Zinkl. 1973. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin upon hemostasis and hematologic function in the rat. *Environmental Health Perspectives* 5:119-23.

5. Zinkl, J.G., J.G. Vos, J.A. Moore, and B.N. Gupta. 1973. Hematologic and clinical chemistry effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin in laboratory animals. *Environmental Health Perspectives* 5:111-8.

6. Vos, J.G., J.A. Moore, and J.G. Zinkl. 1973. Effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin on the immune system of laboratory animals. *Environmental Health Perspectives* 5:149-62.

7. Vos, J.G., J.A. Moore, and J.G. Zinkl. 1974. Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in C57B1/6 mice. *Toxicology and Applied Pharmacology* 29:229-41.

8. Kerkvliet, N.I., and J.A. Oughton. 1993. Acute inflammatory response to sheep red blood cell challenge in mice treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD): Phenotypic and functional analysis of peritoneal exudate cells. *Toxicology and Applied Pharmacology* 119:248-57.

9. Luster, M.I., L.H. Hong, G.A. Boorman, G. Clark, H.T. Hayes, W.F. Greenlee, K. Dold, and A.N. Tucker. 1985. Acute myelotoxic responses in mice exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicology and Applied Pharmacology* 81:156-65.

10. Tucker, A.N., S.J. Vore, and M.I. Luster. 1986. Suppression of B cell differentiation by 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Molecular Pharmacology* 29:372-7.

11. Luster, M.I., J.A. Blank, and J.H. Dean. 1987. Molecular and cellular basis of chemically induced immunotoxicity. *Annual Review of Pharmacology and Toxicology* 27:23-49.

12. Silbergeld, E.K., and T.A. Gasiewicz. 1989. Dioxins and the Ah receptor. *American Journal of Industrial Medicine* 16:455-74.

13. Assennato, G., D. Cervino, E.A. Emmett, G. Longo, and F. Merlo. 1989. Follow-up of subjects who developed chloracne following TCDD exposure at Seveso. *American Journal of Industrial Medicine* 16:119-25.

14. Assennato, G., P. Cannatelli, E. Emmett, I. Ghezzi, and F. Merlo. 1989. Medical monitoring of dioxin clean-up workers. *American Industrial Hygiene Association Journal* 50:586-92.

15. Bertazzi, P.A., I. Bernucci, G. Brambilla, D. Consonni, and A.C. Pesatori. 1998. The Seveso studies on early and long-term effects of dioxin exposure: A review. *Environmental Health Perspectives* 106(Suppl 2):625-33.

16. Bertazzi, P.A. 1991. Long-term effects of chemical disasters. Lessons and results from Seveso. *Science of the Total Environment* 106:5-20.

17. Bertazzi, P.A., C. Zocchetti, A.C. Pesatori, S. Guercilena, M. Sanarico, and L. Radice. 1989. Ten-year mortality study of the population involved in the Seveso incident in 1976. *American Journal of Epidemiology* 129:1187-200.

18. Bertazzi, P.A., C. Zocchetti, A.C. Pesatori, S. Guercilena, M. Sanarico, and L. Radice. 1989. Mortality in an area contaminated by TCDD following an industrial incident. *La Medicina del Lavoro* 80:316-29.

19. Evans, R.G., K.B. Webb, A.P. Knutsen, S.T. Roodman, D.W. Roberts, J.R. Bagby, W.A. Garrett, Jr., and J.S. Andrews, Jr. 1988. A medical follow-up of the health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Archives of Environmental Health* 43:273-8.

20. Hoffman, R.E., P.A. Stehr-Green, K.B. Webb, R.G. Evans, A.P. Knutsen, W.F. Schramm, J.L. Staake, B.B. Gibson, and K.K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *The Journal of the American Medical Association* 255:2031-8.

21. Pocchiari, F., V. Silano, and A. Zampieri. 1979. Human health effects from accidental release of tetrachlorodibenzo-p-dioxin (TCDD) at Seveso, Italy. *Annals of the New York Academy of Science* 320:311-20.

22. Signorini, S., P.M. Gerthoux, C. Dassi, M. Cazzaniga, P. Brambilla, N. Vincoli, and P. Mocarelli. 2000. Environmental exposure to dioxin: The Seveso experience. *Andrologia* 32:263-70.

23. Stehr, P.A., G. Stein, K. Webb, W. Schramm, W.B. Gedney, H.D. Donnell, S. Ayres, H. Falk, E. Sampson, and S.J. Smith. 1986. A pilot epidemiologic study of possible health effects associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin contaminations in Missouri. *Archives of Environmental Health* 41:16-22.

24. Stehr-Green, P.A., R.E. Hoffman, K. Webb, R.G. Evans, A.P. Knutsen, W. Schramm, J.L. Staake, B.B. Gibson, and K.K. Steinberg. 1987. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Chemosphere* 16:2089-94.

25. Webb, K., R.G. Evans, P. Stehr, and S.M. Ayres. 1987. Pilot study on health effects of environmental 2,3,7,8-TCDD in Missouri. *American Journal of Industrial Medicine* 11:685-91.

26. Webb, K.B., R.G. Evans, A.P. Knutsen, S.T. Roodman, D.W. Roberts, W.F. Schramm, B.B. Gibson, J.S. Andrews, Jr., L.K. Needham, and D.G. Patterson. 1989. Medical evaluation of subjects with known body levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 28:183-93.

27. Bond, G.G., M.G. Ott, F.E. Brenner, and R.R. Cook. 1983. Medical and morbidity surveillance findings among employees potentially exposed to TCDD. *British Journal of Industrial Medicine* 40:318-24.

28. Cook, R.R., G.G. Bond, R.A. Olson, and M.G. Ott. 1987. Update of the mortality experience of workers exposed to chlorinated dioxins. *Chemosphere* 16:2111-6.

29. Kogevinas, M., H. Becher, T. Benn, P.A. Bertazzi, P. Boffetta, H.B. Bueno-de-Mesquita, D. Coggon, D. Colin, D. Flesch-Janys, M. Fingerhut, L. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, N. Pearce, and R. Saracci. 1997. Cancer mortality in workers exposed to phenoxy herbicides, chlorophenols, and dioxins. An expanded and updated international cohort study. *American Journal of Epidemiology* 145:1061-75.

30. May, G. 1973. Chloracne from the accidental production of tetrachlorodibenzodioxin. *British Journal of Industrial Medicine* 30:276-83.

31. May, G. 1982. Tetrachlorodibenzodioxin: A survey of subjects ten years after exposure. *British Journal of Industrial Medicine* 39:128-35.

32. Moses, M., R. Lilis, K.D. Crow, J. Thornton, A. Fischbein, H.A. Anderson, and I.J. Selikoff. 1984. Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: Comparison of findings with and without chloracne. *American Journal of Industrial Medicine* 5:161-82.

33. Neuberger, M., C. Rappe, S. Bergek, H. Cai, M. Hansson, R. Jager, M. Kundi, C.K. Lim, H. Wingfors, and A.G. Smith. 1999. Persistent health effects of dioxin contamination in herbicide production. *Environmental Research* 81:206-14.

34. Ott, M.G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.

35. Ott, M.G., R.A. Olson, R.R. Cook, and G.G. Bond. 1987. Cohort mortality study of chemical workers with potential exposure to the higher chlorinated dioxins. *Journal of Occupational Medicine* 29:422-9.

36. Ott, M.G., and A. Zober. 1996. Morbidity study of extruder personnel with potential exposure to brominated dioxins and furans. II. Results of clinical laboratory studies. *Occupational & Environmental Medicine* 53:844-6.

37. Pazderova-Vejlupkova, J., E. Lukas, M. Nemcova, J. Pickova, and L. Jirasek. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Archives of Environmental Health* 36:5-11.

38. Pelclova, D., Z. Fenclova, Z. Dlaskova, P. Urban, E. Lukas, B. Prochazka, C. Rappe, J. Preiss, A. Kocan, and J. Vejlupkova. 2001. Biochemical, neuropsychological, and neurological abnormalities following 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure. *Archives of Environmental Health* 56:493-500.

39. Poland, A.P., D. Smith, G. Metter, and P. Possick. 1971. A health survey of workers in a 2,4-D and 2,4,5-T plan with special attention to chloracne, porphyria cutanea tarda, and psychologic parameters. *Archives of Environmental Health* 22:316-27.

40. Ramlow, J.M., N.W. Spadacene, S.R. Hoag, B.A. Stafford, J.B. Cartmill, and P.J. Lerner. 1996. Mortality in a cohort of pentachlorophenol manufacturing workers, 1940-1989. *American Journal of Industrial Medicine* 30:180-94.

41. Suskind, R.R., and V.S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *The Journal of the American Medical Association* 251:2372-80.

42. Vena, J., P. Boffetta, H. Becher, T. Benn, H.B. Bueno-de-Mesquita, D. Coggon, D. Colin, D. Flesch-Janys, L. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, N. Pearce, A.C. Pesatori, R. Saracci, K. Steenland, and M. Kogevinas. 1998. Exposure to dioxin and nonneoplastic mortality in the expanded IARC international cohort study of phenoxy herbicide and chlorophenol production workers and sprayers. *Environmental Health Perspectives* 106(Suppl 2):645-53.

43. Von Benner, A., L. Edler, K. Mayer, and A. Zober. 1994. ['Dioxin' investigation program of the chemical industry professional organization.] *Arbeitsmedizin Sozialmedizin Praventivmedizin* 29:11-6.

44. Zober, A., M.G. Ott, and P. Messerer. 1994. Morbidity follow up study of BASF employees exposed to 2,3,7, 8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational & Environmental Medicine* 51:479-86.

45. Eisen, S.A., J. Goldberg, W.R. True, and W.G. Henderson. 1991. A co-twin control study of the effects of the Vietnam War on the self-reported physical health of veterans. *American Journal of Epidemiology* 134:49-58.

46. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline morbidity study results. NTIS: AD A 138 340. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

47. Lathrop, G.D., S.G. Machado, T.G. Karrison, W.D. Grubbs, W.F. Thomas, W.H. Wolfe, J.E. Michalek, J.C. Miner, and M.R. Peterson. 1987. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188 262. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

48. Thomas, W.F., W.D. Grubbs, T.G. Karrison, M.B. Lustik, R.H. Roegner, D.E. Williams, W.H. Wolfe, J.E. Michalek, J.C. Miner, and R.W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

49. Roegner, R.H., W.D. Grubbs, M.B. Lustik, A.S. Brockman, S.C. Henderson, D.E. Williams, W.H. Wolfe, J.E. Michalek, and J.C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

50. Grubbs, W.D., W.H. Wolfe, J.E. Michalek, D.E. Williams, M.B. Lustik, A.S. Brockman, S.C. Henderson, F.R. Burnett, R.G. Land, D.J. Osborne, V.K. Rocconi, M.E. Schreiber, J.C. Miner, G.L. Henriksen, and J.A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1992 followup examination results. NTIS: AD A 304 306, 304 308-316. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

51. Michalek, J.E., F.Z. Akhtar, M.P. Longnecker, and J.E. Burton. 2001. Relation of serum 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) level to hematological examination results in veterans of Operation Ranch Hand. *Archives of Environmental Health* 56:396-405.

52. Wolfe, W.H., J.E. Michalek, J.C. Miner, A. Rahe, J. Silva, W.F. Thomas, W.D. Grubbs, M.B. Lustik, T.G. Karrison, R.H. Roegner, and D.E. Williams. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. I. Physical health. *The Journal of the American Medical Association* 264:1824-31.

53. Wolfe, W.H., G.D. Lathrop, R.A. Albanese, and P.M. Moynahan. 1985. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides and associated dioxins. *Chemosphere* 14:707-16.

54. Wolfe, W.H., J.E. Michalek, J.C. Miner, R.H. Roegner, W.D. Grubbs, M.B. Lustik, A.S. Brockman, S.C. Henderson, and D.E. Williams. 1992. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides. Serum dioxin analysis of 1987 examination results. *Chemosphere* 25:213-6.

55. U.S. Centers for Disease Control. 1988. Health status of Vietnam veterans. II. Physical Health. The Centers for Disease Control Vietnam Experience Study. *The Journal of the American Medical Association* 259:2708-14.

56. Takata, T. 2003. Survey on the health effects of chronic exposure to dioxins and its accumulation on workers of a municipal solid waste incinerator, rural part of Osaka Prefecture, and the results of an extended survey afterwards. *Industrial Health* 41:189-96.

57. Hooiveld, M., D.J. Heederik, M. Kogevinas, P. Boffetta, L.L. Needham, D.G. Patterson, Jr., and H.B. Bueno-de-Mesquita. 1998. Second follow-up of a Dutch cohort occupationally exposed to phenoxy herbicides, chlorophenols, and contaminants. *American Journal of Epidemiology* 147:891-901.

58. U.S. Centers for Disease Control. 1989. Health status of Vietnam veterans. Vietnam Experience Study. U.S. Department of Health and Human Services: Atlanta, GA.

59. Kim, H.A., E.M. Kim, Y.C. Park, J.Y. Yu, S.K. Hong, S.H. Jeon, K.L. Park, S.J. Hur, and Y. Heo. 2003. Immunotoxicological effects of Agent Orange exposure to the Vietnam War Korean veterans. *Industrial Health* 41:158-66.

60. Kim, J.S., H.S. Lim, S.I. Cho, H.K. Cheong, and M.K. Lim. 2003. Impact of Agent Orange exposure among Korean Vietnam veterans. *Industrial Health* 41:149-57.

61. Garrow, J.S., and J. Webster. 1985. Quetelet's index (W/H^2) as a measure of fatness. *International Journal of Obesity* 9:147-53.

62. Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L. R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

63. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57(6):369-78

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17 RENAL ASSESSMENT

17.1 INTRODUCTION

17.1.1 Background

17.1.1.1 Organs/Diseases

The Air Force Health Study (AFHS) examinations included several laboratory measures of renal function and a questionnaire to ascertain historic renal disease among participants. The laboratory assessment quantified urinary protein, urine specific gravity, hematuria, leukocyturia, serum creatinine, urinary creatinine, blood urea nitrogen, and microalbumin. The questionnaire provided data that identified participants with a history of kidney disease, defined as kidney trouble, kidney stones, or kidney infections. Similar parameters were investigated in the few epidemiologic studies that assessed dioxin-related renal disease. Occupational and environmental toxins have been associated with acute and chronic renal damage. Heavy metals, such as lead and cadmium, and organic solvents, such as ethylene glycol, have been linked to renal effects ranging from subclinical proteinuria to chronic renal failure (1).

17.1.1.2 Toxicology

In humans, there is little or no evidence that the kidney is a target organ for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin) toxicity. Although renal excretion of phenoxy herbicides (dioxin and 2,4,5-trichlorophenoxyacetic acid [2,4,5-T]) has been well established in animals (2) and humans (3, 4), other studies indicate that it may be of secondary importance to intestinal elimination (5, 6). In addition, more recent reports indicate that the primary route for elimination of dioxin is feces, with only small amounts excreted in urine (7, 8).

Several studies have focused on the renal sequelae of dioxin toxicity in laboratory animals (9-13). In a study of dioxin toxicity in guinea pigs, a decrease in kidney weight was noted relative to controls, and histopathologic examination revealed focal mineralization changes in the renal parenchyma (9). Developmental renal anomalies, including hydronephrosis in mice (10-12) and hamsters (13), occurred after maternal dioxin exposure at toxic levels. In one study, these effects were limited to an aryl hydrocarbon (Ah) receptor-responsive strain (10).

Bowes and Ramos (14) studied rat kidney in vitro cytotoxic responses to several aromatic hydrocarbons, including dioxin, and found that exposed glomerular mesangial cells showed increased deoxyribonucleic acid (DNA) synthetic rates. A subsequent study reported that dioxin-induced mitochondrial membrane injury in both glomerular mesangial cells and tubular epithelial cells of rat kidney demonstrated alterations in glutathione (GSH) status, which is an integral part of cellular antioxidant defense mechanisms (15). Mice exposed to subchronic low doses of dioxin exhibited depletion of GSH in renal tissue, indicative of oxidative stress (16). Other researchers have reported dioxin-stimulated prostaglandin synthesis in canine kidney, which suggests a role in immunotoxicity (17). A report by the Institute of Medicine (IOM) (18) states that the kidney does not appear to be a target organ for dioxin toxicity in animals.

17.1.1.3 Epidemiology

Morbidity studies of humans exposed to dioxin have not emphasized nonmalignant renal and urinary tract disease, although an isolated case of hemorrhagic cystitis occurred in a child exposed to high concentrations of dioxin in soil (19). Epidemiologic studies of populations heavily exposed to dioxin through environmental contamination in Missouri and Seveso, Italy (20-23), including recent updates of the Seveso cohort that evaluated long-term effects (24-26), failed to document any adverse renal effects.

A small study of Times Beach, Missouri, area residents who were exposed to dioxin through contaminated waste oil sprayed at various sites for dust control included various laboratory tests that compared a high-risk group to a low-risk group (27). The high-risk group reported more urinary tract problems than the low-risk group and had higher levels of both occult blood (red blood cells [RBCs]) and white blood cells (WBCs) in urine, though none of the differences reached statistical significance. Another study focusing on residents of the most highly contaminated sites reported no differences on routine urinalysis parameters when compared to an unexposed group (28).

The mortality experience of several cohorts occupationally exposed to dioxin found no indication of excess mortality due to nonmalignant renal disease (29-33). Fewer occupational studies have investigated morbidity outcomes. Clinical examinations were conducted on 204 U.S. workers exposed to dioxin as a contaminant in the manufacturing process of 2,4,5-T from 1948 to 1969, including workers exposed during an industrial accident in 1949 (34). Investigators compared exposed workers to unexposed workers and reported no evidence of renal damage. Zober and colleagues (35) assessed the long-term morbidity experience of 158 German men exposed to dioxin during an accident in 1953, as well as during the subsequent cleanup. When dioxin-exposed workers were compared to unexposed workers, no significant differences were found in the frequency of nephritis and nephrosis or kidney and ureter calculi. A study of persistent health effects of dioxin exposure among 159 Austrian workers exposed 30 years earlier to dioxin did not report any long-term renal effects (36).

Studies of veterans potentially exposed to dioxin in Southeast Asia (SEA) have yielded similarly negative findings. One large study of Vietnam veterans who served in SEA reported that these veterans did not differ in the frequency of kidney disease when compared to veterans who served elsewhere (37). Another large study conducted by the Centers for Disease Control and Prevention (CDC) compared the physical health of Vietnam veterans to non-Vietnam veterans, finding no differences in urinary tract complaints at medical examination (38). Mortality studies of Vietnam-era veterans have not reported excess mortality due to nonmalignant renal disease (39-42), including the mortality update of the Ranch Hand cohort published in 1998 (43).

Prior AFHS reports, which established the body burden of dioxin by serum levels, found no significant differences in standard indices of renal function between the Ranch Hand and Comparison cohorts (44, 45). Routine microscopic urinalysis, however, revealed that there was a higher prevalence of microhematuria among Ranch Hands in the high initial serum dioxin category than among Comparison participants (44), a finding that persisted in the 1992 examination results (46). Though in clinical practice such hematuria is usually of benign origin, the possibility of occult dioxin-induced renal disease was raised.

A recent review of the human health effects of dioxin concluded that there was little evidence that dioxin exposure is related to adverse renal or bladder effects in humans or animals (47). Nonmalignant renal disease in humans has not been evaluated in the IOM's series of *Veterans and Agent Orange* reports (18, 48-51).

17.1.2   Summary of Previous Analyses of the AFHS

17.1.2.1   1982 Baseline Examination Summary Results

The 1982 baseline examination assessed renal disease and function by questionnaire and laboratory testing. Based on questionnaire information, the Ranch Hand group reported significantly more kidney disease than the Comparison group (p=0.039), but this finding was not substantiated by laboratory test results, even when all abnormalities in blood urea nitrogen, creatinine clearance, presence of occult blood, five or more urinary WBCs per high-powered field (HPF), and the presence of urine protein were summed. The distributions of creatinine clearance levels were similar for the two groups, as were the means of blood urea nitrogen, urine specific gravity, and urine WBC count. Difficulty in assessing the degree and significance of hidden noncompliance to the full 24-hour urine collection made the interpretation of the creatinine clearance test results somewhat problematic. Known noncompliance to urine collection, as determined by direct questioning at the end of the sample collection, was much more frequent (p<0.001) in the older participants.

Overall, the baseline examination renal assessment suggested an excess of historical kidney disease in the Ranch Hand group not corroborated by laboratory urinalysis testing.

17.1.2.2   1985 Follow-up Examination Summary Results

A historical assessment of kidney disease and kidney stones by a review-of-systems questionnaire showed no significant differences between the Ranch Hand and Comparison groups. Current renal function was evaluated by five laboratory variables: urine protein, urinary occult blood, urine WBC counts, blood urea nitrogen, and urine specific gravity. Invasive procedures were not used.

The prevalence rates for hematuria were similar for both the Ranch Hand and Comparison groups. The approximate tenfold increase in hematuria in both groups over that observed at the baseline examination was most likely due to different laboratory techniques (reagent-strip testing versus microscopic observation). Similar results were found for leukocyturia. The blood urea nitrogen results were similar to those observed at the baseline examination.

In contrast to the baseline examination values, the 1985 follow-up examination urine specific gravities were lower, a finding most likely attributable to differences in laboratory methodology (falling drop method versus multistick procedure).

In conclusion, all renal measurements, except reported kidney disease, revealed group-by-covariate interactions in the adjusted analyses. These interactions were often complex, making it impossible to reach a firm conclusion as to the presence of a group difference.

17.1.2.3   1987 Follow-up Examination Summary Results

In general, none of the variables of reported history of kidney disease or kidney stones, urinary protein, urinary occult blood, urinary WBCs, blood urea nitrogen, and urine specific gravity showed a significant difference between the two groups for adjusted analyses in the 1987 follow-up examination. Examination of the group-by-covariate interactions did not yield a consistent pattern to suggest renal detriment to either the Ranch Hands or the Comparisons. Lack of a group difference in the reported history of kidney disease or kidney stones (consistent with the 1985 examination results) was in contrast with the baseline examination findings, in which Ranch Hands reported significantly more disease. In the longitudinal analysis of blood urea nitrogen, no difference in the change over time was detected.

17.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Examination Summary Results

The different sets of statistical analyses performed for the renal assessment did not indicate that an association existed between the serum dioxin levels of AFHS participants and their 1987 examination health status. No significant associations with dioxin were observed in the longitudinal analyses of blood urea nitrogen. For some adjusted analyses, diabetic class was a significant covariate in the model. Because dioxin may influence diabetic status, ancillary models without diabetic class also were examined. For the most part, deletion of diabetic class from an adjusted model had no appreciable effect on the outcome of the analysis.

17.1.2.5 1992 Follow-up Examination Summary Results

The analysis of renal health endpoints revealed isolated statistically significant findings, but did not reveal consistent evidence for any detriment related to group membership, estimated initial dioxin exposure, or 1987 serum dioxin levels. One finding that deserved scrutiny was the higher prevalence of urinary occult blood (microhematuria) for Ranch Hands in the high dioxin category relative to the Comparison group. This was consistent with the significant positive dose-response relation between microhematuria and initial dioxin levels (Ranch Hands only) noted in the results of the 1987 examination. None of the other 1992 exposure analysis results, however, was statistically significant for urinary occult blood, and the longitudinal analyses indicate that the prevalence of microhematuria has decreased in the Ranch Hand cohort at each of the last two follow-up examinations. Clinically, the detection of urinary occult blood may signal the presence of silent renal calculi or neoplastic disease. The analyses of kidney stones did not support the presence of silent renal calculi.

17.1.2.6   1997 Follow-up Examination Summary Results

Renal endpoints were not analyzed statistically for the 1997 AFHS follow-up examination report.

17.1.3 Parameters for the 2002 Renal Assessment

17.1.3.1 Dependent Variables

The renal assessment was based on laboratory data collected at the 2002 physical examination, as well as a verified history of kidney stones and kidney disease, as reported by the participant and subsequently verified by a medical records review.

17.1.3.1.1 Medical Records Variables

In the self-administered family and personal history questionnaire, each AFHS participant was asked whether he had ever experienced kidney trouble or kidney stones in the years prior to the 2002 physical examination. Medical records review was accomplished to confirm reported problems with kidney function and to identify any unreported kidney problems for each participant that attended the 2002 physical examination. These data from the 2002 physical examination were combined with data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations to form a complete history of kidney problems for each participant. Based on the verified data, occurrence of kidney stones (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] codes 592.0 - 592.1) and occurrence of past kidney disease (ICD-9-CM codes 271.4, 580.0 – 593.9, 753.0 - 753.4, 788.0, 791.0 – 791.3, 791.6 – 791.9, and operations or procedures 55.01 - 56.99) were classified as "yes" or "no." Predominate conditions for past kidney disease included kidney stone, unspecified disorders of the kidney and ureter, and nonspecific findings on the examination of the urine.

The analyses performed in this chapter were based on the 1,951 participants who attended the 2002 follow-up examination.

Participants with occurrences of kidney disease or kidney stones before duty in SEA were excluded from the analyses of the respective variables.

17.1.3.1.2 Laboratory Variables

Renal variables were quantified by laboratory tests to assess nonspecific renal system function. Urinary protein and urine specific gravity were determined by accepted dipstick methods using Bayer Atlas® equipment. Hematuria and leukocyturia were measured by high-powered microscopic examination. Serum creatinine, urinary creatinine, and blood urea nitrogen were assayed using Dade Behring Dimension® RxL equipment. Urinary microalbumin was assayed using the Beckman Coulter IMMAGE® system.

An empirical formula, based on age, body weight, and serum creatinine, was used to estimate creatinine clearance without using a timed collection of urine. The formula used was

$$[(140 - age\ (years)) \times weight\ (kg)]/[serum\ creatinine\ (mg/dL) \times 72]\ (52\text{-}54).$$

Low creatinine clearance was considered to be undesirable because of the inverse relation with high serum creatinine levels. Blood urea nitrogen (mg/dL), serum creatinine (mg/dL), creatinine clearance, and urine specific gravity were analyzed as continuous variables. Hematuria (urinary RBCs per HPF) (≤ 2, >2), leukocyturia (urinary WBCs per HPF) (≤ 2, >2), and urinary protein (absent, present) were analyzed as dichotomous variables.

A urinary microalbumin to urinary creatinine ratio helps adjust the microalbumin measure for the factors that lead to variability. This ratio also is substantially better than a microalbumin measure alone for identifying patients at risk for early kidney damage secondary to diabetes. The urinary microalbumin to urinary creatinine ratio ($\mu g/mg$) had a large number of measurements (87%) equal to 0, indicating no microalbumin in the participant's urine. The nonzero measurements exhibited a positively skewed distribution, so a logarithmic transformation was applied to achieve an approximate normal distribution. The logarithmic transformation, however, could not be applied to the measurements equal to 0. Consequently, this variable was analyzed in two forms: (1) an analysis based on the continuous form of the nonzero measurements and (2) an analysis based on a discrete form of the urinary microalbumin to urinary creatinine ratio, where the proportion of nonzero measurements was analyzed.

No participants were excluded for medical reasons from the analysis of these variables.

17.1.3.2 Covariates

Age, race, military occupation, and diabetic status were used as covariates in adjusted statistical analyses evaluating all renal dependent variables. Age, race, and military occupation were determined from military records.

In the 2002 questionnaire, a general screening question on diabetes was posed. During the in-person health interview each participant was asked: "Since the date of the last interview, has a doctor told you for the first time that you had diabetes?" Medical records review was accomplished to confirm reported diabetes and to identify any unreported diabetes for each participant that attended the 2002 physical examination. These data from the 2002 physical examination were combined with data from the 1982

baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations to form a complete history of diabetes for each participant. The analyses performed in this chapter were based on the 1,951 participants who attended the 2002 follow-up examination. Participants with a verified history of diabetes, as diagnosed previously by a physician, were combined with those participants with either

- a 2-hour postprandial glucose level of 200 mg/dL or greater on two separate occasions

- a fasting glucose level of 126 mg/dL or greater on two separate occasions, or

- one 2-hour postprandial glucose measurement ≥200 mg/dL and one fasting glucose ≥126 mg/dL on two separate occasions,

and classified as "diabetic" for the diabetic class covariate. Those participants not classified as "diabetic," as defined above, but with a 2-hour postprandial glucose level of at least 140 mg/dL or a fasting glucose level of at least 110 mg/dL at the 2002 physical examination, were classified as "impaired." Those participants not classified as "diabetic" or "impaired" as defined above were classified as "normal."

Analyses of the urinary microalbumin to urinary creatinine ratio included four additional covariates: taking a calcium channel blocker (yes/no), taking an angiotensin converting enzyme (ACE) inhibitor (yes/no), taking an alpha- or beta-adrenergic blocking agent (yes/no), and taking a diuretic (yes/no) at the time of the 2002 AFHS physical examination.

17.1.4 Statistical Methods

Table 17-1 summarizes the statistical analysis performed for the 2002 renal assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, exclusions, and statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 17-1.

Table 17-1. Statistical Analysis for the Renal Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Occurrence of Kidney Stones	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Occurrence of Past Kidney Disease	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Blood Urea Nitrogen (mg/dL)	LAB	C	--	(1)	None	U:GLM,TT A:GLM
Serum Creatinine (mg/dL)	LAB	C	--	(1)	None	U:GLM,TT A:GLM
Creatinine Clearance (calculated)	LAB/PE/MIL	C	--	(1)	None	U:GLM,TT A:GLM

Table 17-1. Statistical Analysis for the Renal Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Urinary Microalbumin to Urinary Creatinine Ratio (µg/mg)	LAB	C/D	Nonzero Zero	(2)	None	U:GLM,TT A:GLM
Urine Specific Gravity	LAB	C	--	(1)	None	U:GLM,TT A:GLM
Urinary Occult Blood (cells/HPF)	LAB	D	Abnormal: >2 Normal: ≤2	(1)	None	U:LR,CS A:LR
Urinary WBC Count (cells/HPF)	LAB	D	Abnormal: >2 Normal: ≤2	(1)	None	U:LR,CS A:LR
Urinary Protein	LAB	D	Present Absent	(1)	None	U:LR,CS A:LR

[a]Covariates:

(1) age, race, military occupation, diabetic class.

(2) age, race, military occupation, diabetic class, calcium channel blocker use, ACE inhibitor use, alpha- or beta-adrenergic blocking agent use, diuretic use.

[b]Exclusions:

(a) participants with a pre-SEA history of the corresponding condition.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	C/D	Born ≥ 1942 Born < 1942
Race	MIL	D	Black Non-Black
Military Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Calcium Channel Blocker Use at the Time of the 2002 Physical Examination	MR-V	D	Yes No
ACE Inhibitor Use at the Time of the 2002 Physical Examination	MR-V	D	Yes No
Alpha- or Beta-adrenergic Blocking Agent Use at the Time of the 2002 Physical Examination	MR-V	D	Yes No
Diuretic Use at the Time of the 2002 Physical Examination	MR-V	D	Yes No

Table 17-1. Statistical Analysis for the Renal Assessment (Continued)

Variable (Units)	Data Source	Data Form	Cutpoints
Diabetic Class	LAB/MR-V	D	• Diabetic: past history of diabetes, as diagnosed previously by a physician, or ≥200 mg/dL 2-hour postprandial glucose on two separate occasions, or ≥126 mg/dL fasting glucose on two separate occasions, or one 2-hour postprandial glucose measurement ≥200 mg/dL and one fasting glucose ≥126 mg/dL on two separate occasions • Impaired: not diabetic; ≥140 mg/dL 2-hour postprandial glucose or ≥110 mg/dL fasting glucose at the 2002 physical examination • Normal: not diabetic or impaired; <140 mg/dL 2-hour postprandial glucose and <110 mg/dL fasting glucose at the 2002 physical examination

Abbreviations

Data Source:	LAB: 2002 laboratory results
	MIL: Air Force military records
	MR-V: Medical records (verified)
	PE: 2002 physical examination
Data Form:	C: Continuous form of dependent variable
	D: Discrete form of dependent variable or covariate
	C/D: Continuous and discrete forms of dependent variable; appropriate form for analysis (either continuous or discrete) of covariate
Statistical Analysis:	U: Unadjusted analysis
	A: Adjusted analysis
Statistical Methods:	CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
	GLM: General linear models analysis
	LR: Logistic regression analysis
	TT: Two-sample t-test

Four models were examined for each dependent variable given in Table 17-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for covariates. These covariates are given in Table 17-1. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. In an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-4, the median level of exposure to dioxin was highest for enlisted groundcrew, followed by enlisted flyers, then officers.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the CDC using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in

parts per trillion (ppt) on a lipid weight basis (55). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2. A statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model to account for body mass index-related differences in elimination rate (56).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. Another category was examined by combining the low and high Ranch Hand categories. This combination is referred to in the tables as the "low plus high Ranch Hand" category. These five categories—Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the four Ranch Hand categories and the dependent variable in the Comparison category was examined. As in Model 2, a statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables. One Ranch Hand without a dioxin measure was excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The term "unadjusted" was used in the text and tables as follows: Models 1 and 4 did not adjust for any covariates. Models 2 and 3 adjusted only for body mass index at the time of the blood measurement for dioxin. The term "adjusted" was used in the text and tables as follows: Models 1 and 4 adjusted for the covariates shown in Table 17-1 unless otherwise specified by a footnote to the table. Models 2 and 3 additionally adjusted only for body mass index at the time of the blood measurement for dioxin.

Table 17-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants that were excluded from analyses is given.

Table 17-2. Number of Participants Excluded or with Missing Data for the Renal Assessment

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Pre-SEA History of Kidney Stones	EXC	9	12	5	9	9	12
Pre-SEA History of Kidney Disease	EXC	14	21	7	13	13	21
Creatinine Clearance	DEP	1	0	0	1	1	0

[a]777 Ranch Hands and 1,174 Comparisons for group.
[b]424 Ranch Hands for initial dioxin; 776 Ranch Hands for 1987 dioxin.
[c]776 Ranch Hands and 1,174 Comparisons for categorized dioxin.

Note: DEP = Dependent variable.
EXC = Exclusion.

17.2 RESULTS

17.2.1 Dependent Variable-covariate Associations

The renal dependent variables were tested for associations with each of the covariates used in the adjusted analyses. The complete results are presented in Appendix F, Table F-9. These associations were pairwise between the dependent variable and the covariate and were not adjusted for any other covariates. The following paragraphs summarize the pattern of significant ($p \leq 0.05$) dependent variable-covariate associations. In the discussion of the results, low levels were considered adverse for creatinine clearance.

Older participants had more occurrences of kidney stones and kidney disease than did younger participants. Creatinine clearance and urine specific gravity each decreased with age. Blood urea nitrogen and serum creatinine increased with age. For participants with urinary microalbumin present, the urinary microalbumin to urinary creatinine ratio increased with age.

All dependent variables except for the continuous form of the urinary microalbumin to urinary creatinine ratio were associated with race. Non-Black participants had more occurrences of kidney stones than did Black participants, but fewer occurrences of kidney disease than Black participants. Black participants had higher mean values for serum creatinine and urine specific gravity than Non-Black participants. A higher percentage of Black participants had urinary microalbumin present than did non-Black participants. In addition, Black participants had a higher prevalence of abnormal results for urinary occult blood, urinary WBC count, and urinary protein than non-Black participants. Mean blood urea nitrogen and creatinine clearance levels were higher for Non-Black participants that Black participants.

Military occupation was associated with blood urea nitrogen, serum creatinine, creatinine clearance, urine specific gravity, and the ratio of urinary microalbumin to urinary creatinine in its discrete form. Officers had higher mean blood urea nitrogen and serum creatinine levels than enlisted personnel, but a lower mean creatinine clearance and urine specific gravity. A larger percentage of enlisted personnel than officers had urinary microalbumin present.

Diabetic participants had the highest mean blood urea nitrogen and serum creatinine levels. For participants with urinary microalbumin present, diabetic participants also had the highest mean urinary

microalbumin to urinary creatinine ratio. In addition, diabetic participants had the highest prevalence of kidney disease and urinary protein, and the greatest proportion of participants with urinary microalbumin present was found among diabetics. Participants in the impaired diabetic class had the most occurrences of kidney stones, followed by diabetic participants, then participants with normal glucose levels.

Use of calcium channel blockers, ACE inhibitors, and diuretics at the time of the physical examination were associated with the percentage of participants with urinary microalbumin present. For participants with urinary microalbumin present, these medications also were associated with the urinary microalbumin to urinary creatinine ratio. Urinary microalbumin was present more often in participants taking these medications than in participants who were not taking these medications. In addition, a higher mean urinary microalbumin to urinary creatinine ratio was observed for participants taking these medications than for participants who were not. The mean urinary microalbumin to urinary creatinine ratio was higher in participants who used alpha- or beta-adrenergic blocking agents at the time of the physical exam than for participants who did not use this type of medication.

17.2.2   Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 17-1. Dependent variables are grouped into two sections: (1) the questionnaire variables, derived from the questionnaire that was administered in the 2002 follow-up and previous AFHS examinations, and (2) the laboratory examination variables, obtained during the 2002 physical examination.

17.2.2.1 Medical Records Variables

17.2.2.1.1 Occurrence of Kidney Stones

Model 1 showed no significant difference in occurrence of kidney stones between Ranch Hands and Comparisons in either the unadjusted or adjusted analysis (Table 17-3(a,b): p>0.13 for all contrasts). A significant inverse association between the occurrence of kidney stones and initial dioxin was seen in the unadjusted Model 2 analysis (Table 17-3(c): Unadjusted Relative Risk [RR]=0.72, p=0.008). After adjusting for covariates, the results were nonsignificant (Table 17-3(d): p=0.059).

The unadjusted Model 3 analysis of occurrence of kidney stones showed a significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 17-3(e): Unadjusted RR=1.58, p=0.033). The same contrast was nonsignificant after adjusting for covariates (Table 17-3(f): p=0.053). No significant differences in the occurrence of kidney stones were found between Ranch Hands in the high dioxin category or low and high dioxin categories combined and Comparisons in the unadjusted and adjusted Model 3 analyses (Table 17-3(e,f): p>0.40 for each analysis). No significant relations were shown between occurrence of kidney stones and 1987 dioxin in the unadjusted or adjusted Model 4 analyses (Table 17-3(g,h): p>0.39 for each analysis).

Table 17-3. Analysis of Occurrence of Kidney Stones

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*86 (11.2)*	*1.11 (0.82,1.48)*	*0.505*
	Comparison	*1,162*	*119 (10.2)*		
Officer	Ranch Hand	303	42 (13.9)	1.40 (0.90,2.18)	0.137
	Comparison	456	47 (10.3)		
Enlisted Flyer	Ranch Hand	132	15 (11.4)	0.99 (0.49,2.00)	0.975
	Comparison	183	21 (11.5)		
Enlisted Groundcrew	Ranch Hand	333	29 (8.7)	0.88 (0.55,1.42)	0.610
	Comparison	523	51 (9.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*1.09 (0.81,1.47)*	*0.558*
Officer	759	1.37 (0.88,2.14)	0.169
Enlisted Flyer	315	0.98 (0.48,1.99)	0.961
Enlisted Groundcrew	856	0.89 (0.55,1.44)	0.634

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	23 (16.5)	0.72 (0.56,0.93)	0.008**
Medium	140	15 (10.7)		
High	140	12 (8.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
419	0.76 (0.57,1.02)	0.059

[a]Relative risk for a twofold increase in initial dioxin.

Table 17-3. Analysis of Occurrence of Kidney Stones (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,162	119 (10.2)		
Background RH	348	36 (10.3)	1.03 (0.69,1.54)	0.873
Low RH	208	32 (15.4)	1.58 (1.04,2.42)	0.033*
High RH	211	18 (8.5)	0.80 (0.48,1.35)	0.408
Low plus High RH	419	50 (11.9)	1.12 (0.78,1.61)	0.525

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,162		
Background RH	348	0.98 (0.65,1.47)	0.927
Low RH	208	1.53 (1.00,2.34)	0.053
High RH	211	0.87 (0.51,1.48)	0.600
Low plus High RH	419	1.15 (0.79,1.66)	0.466

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	258	28 (10.9)	0.94 (0.82,1.08)	0.399
Medium	255	35 (13.7)		
High	254	23 (9.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 17-3. Analysis of Occurrence of Kidney Stones (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
767	0.99 (0.83,1.17)	0.877

[a]Relative risk for a twofold increase in 1987 dioxin.

17.2.2.1.2 Occurrence of Past Kidney Disease

All unadjusted and adjusted analyses of occurrence of kidney disease for Models 1 through 4 were nonsignificant (Table 17-4(a-h): p>0.10 for all analyses).

Table 17-4. Analysis of Occurrence of Past Kidney Disease

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*763*	*271 (35.5)*	*0.91 (0.75,1.10)*	*0.307*
	Comparison	*1,153*	*436 (37.8)*		
Officer	Ranch Hand	302	104 (34.4)	0.91 (0.67,1.24)	0.558
	Comparison	449	164 (36.5)		
Enlisted Flyer	Ranch Hand	129	53 (41.1)	1.30 (0.82,2.06)	0.273
	Comparison	183	64 (35.0)		
Enlisted Groundcrew	Ranch Hand	332	114 (34.3)	0.79 (0.59,1.05)	0.101
	Comparison	521	208 (39.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,916*	*0.90 (0.75,1.10)*	*0.311*
Officer	751	0.88 (0.65,1.21)	0.436
Enlisted Flyer	312	1.30 (0.81,2.08)	0.280
Enlisted Groundcrew	853	0.81 (0.60,1.08)	0.147

Table 17-4. Analysis of Occurrence of Past Kidney Disease (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	47 (33.8)	1.02 (0.87,1.18)	0.844
Medium	140	48 (34.3)		
High	138	55 (39.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	1.12 (0.93,1.34)	0.238

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,153	436 (37.8)		
Background RH	346	121 (35.0)	0.96 (0.74,1.24)	0.740
Low RH	208	75 (36.1)	0.90 (0.66,1.23)	0.523
High RH	209	75 (35.9)	0.86 (0.63,1.18)	0.350
Low plus High RH	417	150 (36.0)	0.88 (0.70,1.12)	0.299

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 17-4. Analysis of Occurrence of Past Kidney Disease (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,153		
Background RH	346	0.98 (0.75,1.27)	0.882
Low RH	208	0.83 (0.60,1.14)	0.247
High RH	209	0.89 (0.64,1.23)	0.475
Low plus High RH	417	0.86 (0.67,1.09)	0.216

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	85 (33.2)	1.03 (0.94,1.13)	0.488
Medium	255	92 (36.1)		
High	252	94 (37.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
763	1.02 (0.91,1.14)	0.734

[a]Relative risk for a twofold increase in 1987 dioxin.

17.2.2.2 Laboratory Variables

17.2.2.2.1 Blood Urea Nitrogen

The unadjusted and adjusted Model 1 and Model 2 analyses of blood urea nitrogen showed no significant results (Table 17-5(a-d): p>0.05 for each analysis).

The unadjusted Model 3 analysis revealed a significant difference between Ranch Hands in the high dioxin category and Comparisons (Table 17-5(e): difference of means=-0.70 mg/dL, p=0.044). After adjusting for covariates, no contrasts were significant (Table 17-5(f): p>0.22 for each contrast).

The unadjusted and adjusted Model 4 analyses revealed no significant associations between blood urea nitrogen and 1987 dioxin (Table 17-5(g,h): p>0.59 for each analysis).

Table 17-5. Analysis of Blood Urea Nitrogen (mg/dL)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*777*	*16.18*	*-0.34*	*0.127*
	Comparison	*1,174*	*16.52*		
Officer	Ranch Hand	307	16.84	-0.64	0.083
	Comparison	462	17.48		
Enlisted Flyer	Ranch Hand	133	16.19	-0.10	0.852
	Comparison	185	16.29		
Enlisted Groundcrew	Ranch Hand	337	15.60	-0.20	0.528
	Comparison	527	15.80		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*777*	*15.79*	*-0.33*	*0.113*
	Comparison	*1,174*	*16.12*		
Officer	Ranch Hand	307	16.04	-0.64	0.059
	Comparison	462	16.68		
Enlisted Flyer	Ranch Hand	133	15.55	-0.15	0.758
	Comparison	185	15.70		
Enlisted Groundcrew	Ranch Hand	337	15.84	-0.13	0.682
	Comparison	527	15.97		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 17-5. Analysis of Blood Urea Nitrogen (mg/dL) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	140	16.53	16.59	0.036	-0.014 (0.010)	0.185
Medium	143	16.02	16.06			
High	141	15.90	15.81			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of blood urea nitrogen versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	140	16.09	0.094	0.004 (0.012)	0.715
Medium	143	16.16			
High	141	16.31			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of blood urea nitrogen versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,174	16.52	16.51		
Background RH	352	16.29	16.47	-0.04	0.877
Low RH	211	16.32	16.26	-0.25	0.477
High RH	213	15.97	15.81	-0.70	0.044*
Low plus High RH	424	16.15	16.03	-0.48	0.072

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 17-5. Analysis of Blood Urea Nitrogen (mg/dL) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,174	16.06		
Background RH	352	15.73	-0.33	0.239
Low RH	211	15.65	-0.41	0.223
High RH	213	15.95	-0.11	0.749
Low plus High RH	424	15.80	-0.26	0.313

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	260	16.22	<0.001	-0.003 (0.006)	0.628
Medium	258	16.31			
High	258	16.11			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of blood urea nitrogen versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	260	15.87	0.071	0.004 (0.007)	0.596
Medium	258	15.84			
High	258	16.29			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of blood urea nitrogen versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

17.2.2.2.2 Serum Creatinine

Both the unadjusted and adjusted Model 1 analyses of serum creatinine revealed significant overall group differences (Table 17-6(a,b): difference of means=-0.02 mg/dL, p=0.038; difference of adjusted means=-0.02, p=0.031). The overall adjusted mean serum creatinine values were 1.17 mg/dL for Ranch Hands and 1.19 mg/dL for Comparisons. After stratifying by military occupation, unadjusted and adjusted analyses revealed group differences within the officer stratum (unadjusted: difference of means=-0.03 mg/dL, p=0.025; adjusted: difference of adjusted means=-0.04 mg/dL, p=0.010). Among the officers, the Ranch Hands had an adjusted mean serum creatinine value of 1.16 mg/dL versus 1.20 mg/dL for the Comparisons.

The unadjusted Model 2 analysis revealed a significant inverse association between initial dioxin and serum creatinine (Table 17-6(c): Slope=-0.016, p=0.010). After adjusting for covariates, the relation became nonsignificant (Table 17-6(d): p=0.392).

Ranch Hands in the high dioxin category had a significantly lower mean serum creatinine level than Comparisons in the unadjusted Model 3 analysis (Table 17-6(e): difference of means=-0.05 mg/dL, p=0.003). After adjusting for covariates, all contrasts were nonsignificant (Table 17-6(f): p>0.09 for all contrasts).

No significant associations were seen in the unadjusted and adjusted Model 4 analyses of serum creatinine (Table 17-6(g,h): p>0.32 for each analysis).

Table 17-6. Analysis of Serum Creatinine (mg/dL)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*777*	*1.11*	*-0.02*	*0.038**
	Comparison	*1,174*	*1.13*		
Officer	Ranch Hand	307	1.11	-0.03	0.025*
	Comparison	462	1.15		
Enlisted Flyer	Ranch Hand	133	1.13	0.01	0.699
	Comparison	185	1.12		
Enlisted Groundcrew	Ranch Hand	337	1.09	-0.02	0.197
	Comparison	527	1.11		

[a]Transformed from natural logarithm scale.

[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Table 17-6. Analysis of Serum Creatinine (mg/dL) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*777*	*1.17*	*-0.02*	*0.031**
	Comparison	*1,174*	*1.19*		
Officer	Ranch Hand	307	1.16	-0.04	0.010**
	Comparison	462	1.20		
Enlisted Flyer	Ranch Hand	133	1.17	0.01	0.754
	Comparison	185	1.17		
Enlisted Groundcrew	Ranch Hand	337	1.17	-0.02	0.306
	Comparison	527	1.19		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for $\log_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	140	1.14	1.14	0.025	-0.016 (0.006)	0.010**
Medium	143	1.10	1.10			
High	141	1.09	1.08			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of serum creatinine versus $\log_2$ (initial dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 17-6. Analysis of Serum Creatinine (mg/dL) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	140	1.19	0.078	-0.006 (0.007)	0.392
Medium	143	1.17			
High	141	1.17			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of serum creatinine versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,174	1.13	1.13		
Background RH	352	1.11	1.11	-0.02	0.251
Low RH	211	1.13	1.13	0.00	0.886
High RH	213	1.09	1.08	-0.05	0.003**
Low plus High RH	424	1.11	1.10	-0.03	0.060

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 17-6. Analysis of Serum Creatinine (mg/dL) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,174	1.18		
Background RH	352	1.16	-0.02	0.099
Low RH	211	1.17	-0.01	0.503
High RH	213	1.16	-0.02	0.093
Low plus High RH	424	1.17	-0.01	0.117

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	260	1.10	0.001	-0.004 (0.004)	0.326
Medium	258	1.12			
High	258	1.09			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of serum creatinine versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	260	1.17	0.059	-0.002 (0.004)	0.590
Medium	258	1.17			
High	258	1.16			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of serum creatinine versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

17.2.2.2.3 Creatinine Clearance

The unadjusted and adjusted Model 1 analyses of creatinine clearance showed no group differences between Ranch Hands and Comparisons (Table 17-7(a,b): p>0.05 for each analysis). A significant association between creatinine clearance and initial dioxin was seen in the unadjusted Model 2 analysis (Table 17-7(c): Slope=0.132, p=0.001). After adjusting for covariates, however, the relation became nonsignificant (Table 17-7(d): p=0.509).

The unadjusted Model 3 analysis of creatinine clearance revealed two significant contrasts: Ranch Hands in the high dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 17-7(e): difference of means=7.06, p<0.001; difference of means=3.56, p=0.003, respectively). After covariate adjustment, the Model 3 analysis of creatinine clearance revealed a significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 17-7(f): difference of adjusted means=2.92, p=0.015) as well as a significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 17-7(f): difference of adjusted means=2.26, p=0.014). The contrast of Ranch Hands in the high dioxin category versus Comparisons was no longer significant (Table 17-7(f): p=0.188). The adjusted mean creatinine clearance values in the low, combined low and high, and Comparison dioxin categories were 85.27, 84.61, and 82.35, respectively.

The unadjusted and adjusted analyses for Model 4 each showed significant positive associations between creatinine clearance and 1987 dioxin (Table 17-7(g,h): Slope=0.173, p<0.001, unadjusted; adjusted Slope=0.118, p<0.001, adjusted). The adjusted mean creatinine clearance values in the low, medium, and high 1987 dioxin categories were 79.36, 85.48, and 86.92, respectively.

Table 17-7. Analysis of Creatinine Clearance

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*776*	*87.57*	*1.13*	*0.278*
	Comparison	*1,174*	*86.45*		
Officer	Ranch Hand	306	82.88	1.96	0.210
	Comparison	462	80.92		
Enlisted Flyer	Ranch Hand	133	82.67	-3.12	0.202
	Comparison	185	85.79		
Enlisted Groundcrew	Ranch Hand	337	93.97	2.29	0.146
	Comparison	527	91.68		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Table 17-7. Analysis of Creatinine Clearance (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*776*	*85.44*	*1.27*	*0.136*
	Comparison	*1,174*	*84.17*		
Officer	Ranch Hand	306	86.13	2.58	0.059
	Comparison	462	83.55		
Enlisted Flyer	Ranch Hand	133	84.06	-2.06	0.328
	Comparison	185	86.12		
Enlisted Groundcrew	Ranch Hand	337	84.99	1.36	0.289
	Comparison	527	83.63		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	140	85.99	86.57	0.166	0.132 (0.040)	0.001**
Medium	143	92.93	93.24			
High	141	95.60	94.67			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of creatinine clearance versus $\log_2$ (initial dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	140	86.93	0.493	-0.024 (0.036)	0.509
Medium	143	87.79			
High	141	85.44			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of creatinine clearance versus $\log_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 17-7. Analysis of Creatinine Clearance (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,174	86.45	86.31		
Background RH	351	83.02	85.35	-0.96	0.446
Low RH	211	87.24	86.40	0.09	0.957
High RH	213	95.78	93.37	7.06	<0.001**
Low plus High RH	424	91.48	89.87	3.56	0.003**

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,174	82.35		
Background RH	351	83.19	0.84	0.394
Low RH	211	85.27	2.92	0.015*
High RH	213	83.97	1.62	0.188
Low plus High RH	424	84.61	2.26	0.014*

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 17-7. Analysis of Creatinine Clearance (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	259	82.21	0.056	0.173 (0.026)	<0.001**
Medium	258	86.53			
High	258	94.28			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of creatinine clearance versus log_2 (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	259	79.36	0.343	0.118 (0.025)	<0.001**
Medium	258	85.48			
High	258	86.92			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of creatinine clearance versus log_2 (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

17.2.2.2.4 Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero Measurements)

Both the unadjusted and adjusted Model 1 analyses of nonzero urinary microalbumin to urinary creatinine ratio values revealed significant overall group differences (Table 17-8(a,b): difference of means=-11.93 µg/mg, p=0.008; difference of adjusted means=-12.69 µg/mg, p=0.037). The overall adjusted mean ratio of the nonzero values was 27.44 µg/mg and 40.13 µg/mg for Ranch Hands and Comparisons, respectively. After stratifying by military occupation, unadjusted and adjusted analyses revealed group differences within the enlisted groundcrew stratum (unadjusted: difference of means=-17.48 µg/mg, p=0.002; adjusted: difference of adjusted means=-19.06 µg/mg, p=0.024). Within the enlisted groundcrew stratum, the Ranch Hands had an adjusted mean urinary microalbumin to urinary creatinine ratio value of 23.85 µg/mg versus 42.91 µg/mg for the Comparisons.

The association between initial dioxin and the urinary microalbumin to urinary creatinine ratio examined in the unadjusted and adjusted Model 2 analyses revealed nonsignificant results (Table 17-8(c,d): p≥0.30 for each analysis). The unadjusted Model 3 analysis revealed two significant contrasts: Ranch Hands in the low dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories

combined versus Comparisons (Table 17-8(e): difference of means=-12.49 µg/mg, p=0.039; difference of means=-11.26 µg/mg, p=0.024, respectively). After covariate adjustment, the Model 3 analysis revealed a significant difference between Ranch Hands in the low dioxin category and Comparisons (Table 17-8(f): difference of adjusted means=-16.47 µg/mg, p=0.033). Ranch Hands in the low dioxin category had a lower mean urinary microalbumin to urinary creatinine ratio than Comparisons (22.00 µg/mg and 38.47 µg/mg, respectively).

The unadjusted and adjusted Model 4 analyses did not reveal a significant association between urinary microalbumin to urinary creatinine ratio and 1987 dioxin (Table 17-8(g,h): p≥0.39 for each analysis).

Table 17-8. Analysis of Urinary Microalbumin to Urinary Creatinine Ratio (µg/mg) (Nonzero Measurements)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*106*	*17.53*	*-11.93*	*0.008***
	Comparison	*141*	*29.46*		
Officer	Ranch Hand	31	26.18	0.96	0.916
	Comparison	45	25.22		
Enlisted Flyer	Ranch Hand	25	20.40	-16.67	0.174
	Comparison	23	37.07		
Enlisted Groundcrew	Ranch Hand	50	12.68	-17.48	0.002**
	Comparison	73	30.16		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

**: Statistically significant (p-value≤0.010).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*106*	*27.44*	*-12.69*	*0.037**
	Comparison	*141*	*40.13*		
Officer	Ranch Hand	31	33.37	2.33	0.822
	Comparison	45	31.05		
Enlisted Flyer	Ranch Hand	25	26.21	-21.15	0.141
	Comparison	23	47.36		
Enlisted Groundcrew	Ranch Hand	50	23.85	-19.06	0.024*
	Comparison	73	42.91		

[a]Transformed from natural logarithm scale.

[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.

[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < $ p-value ≤ 0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	21	15.94	16.89	0.109	0.038 (0.132)	0.776
Medium	24	17.83	17.82			
High	19	21.15	19.85			

[a]Transformed from natural logarithm scale.

[b]Adjusted for body mass index at the time of the blood measurement of dioxin.

[c]Slope and standard error based on natural logarithm of urinary microalbumin to urinary creatinine ratio versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	21	11.53	0.376	0.163 (0.156)	0.300
Medium	24	12.51			
High	19	18.05			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of urinary microalbumin to urinary creatinine ratio versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	141	29.46	28.54		
Background RH	42	16.73	19.95	-8.59	0.173
Low RH	35	15.98	16.05	-12.49	0.039*
High RH	29	20.99	18.89	-9.65	0.170
Low plus High RH	64	18.08	17.28	-11.26	0.024*

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	141	38.47		
Background RH	42	29.42	-9.05	0.284
Low RH	35	22.00	-16.47	0.033*
High RH	29	30.19	-8.28	0.412
Low plus High RH	64	25.39	-13.08	0.051

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	30	14.01	0.007	0.073 (0.085)	0.390
Medium	36	18.87			
High	40	19.42			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of urinary microalbumin to urinary creatinine ratio versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

Table 17-8. Analysis of Urinary Microalbumin to Urinary Creatinine Ratio (μg/mg) (Nonzero Measurements) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	30	16.07	0.266	0.057 (0.096)	0.553
Medium	36	20.54			
High	40	21.10			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of urinary microalbumin to urinary creatinine ratio versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

17.2.2.2.5 Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero versus Zero)

All unadjusted and adjusted analyses of the percentage of nonzero urinary microalbumin to urinary creatinine ratio measurements were nonsignificant for Models 1 through 4 (Table 17-9(a-h): p>0.09 for each analysis).

Table 17-9. Analysis of Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero versus Zero)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Nonzero	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*106 (13.6)*	*1.16 (0.88,1.52)*	*0.290*
	Comparison	*1,174*	*141 (12.0)*		
Officer	Ranch Hand	307	31 (10.1)	1.04 (0.64,1.69)	0.871
	Comparison	462	45 (9.7)		
Enlisted Flyer	Ranch Hand	133	25 (18.8)	1.63 (0.88,3.02)	0.120
	Comparison	185	23 (12.4)		
Enlisted Groundcrew	Ranch Hand	337	50 (14.8)	1.08 (0.73,1.60)	0.686
	Comparison	527	73 (13.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,951*	*1.18 (0.90,1.56)*	*0.238*
Officer	769	1.03 (0.63,1.68)	0.904
Enlisted Flyer	318	1.71 (0.91,3.23)	0.097
Enlisted Groundcrew	864	1.12 (0.75,1.67)	0.582

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Nonzero	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	21 (15.0)	0.93 (0.76,1.15)	0.509
Medium	143	24 (16.8)		
High	141	19 (13.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
424	0.88 (0.69,1.12)	0.284

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Nonzero	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	141 (12.0)		
Background RH	352	42 (11.9)	1.09 (0.75,1.58)	0.645
Low RH	211	35 (16.6)	1.42 (0.94,2.13)	0.093
High RH	213	29 (13.6)	1.06 (0.69,1.64)	0.782
Low plus High RH	424	64 (15.1)	1.23 (0.89,1.69)	0.216

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,174		
Background RH	352	1.26 (0.86,1.85)	0.243
Low RH	211	1.33 (0.87,2.01)	0.188
High RH	213	0.98 (0.63,1.55)	0.947
Low plus High RH	424	1.14 (0.82,1.59)	0.436

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Nonzero	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	30 (11.5)	1.05 (0.92,1.19)	0.479
Medium	258	36 (14.0)		
High	258	40 (15.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
	Adjusted Relative Risk	
n	(95% C.I.)[a]	p-Value
776	0.94 (0.81,1.09)	0.410

[a]Relative risk for a twofold increase in 1987 dioxin.

17.2.2.2.6 Urine Specific Gravity

The unadjusted and adjusted Model 1 through 3 analyses of urine specific gravity did not show any significant group differences (Table 17-10(a-f): p>0.05 for each analysis). The unadjusted Model 4 analysis revealed a significant positive association between 1987 dioxin and urine specific gravity (Table 17-10(g): Slope=0.0003, p=0.033). After adjusting for covariates, however, the relation became nonsignificant (Table 17-10(h): p=0.807).

Table 17-10. Analysis of Urine Specific Gravity

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*1.0184*	*0.0000 (-0.0006,0.0006)*	*0.979*
	Comparison	*1,174*	*1.0184*		
Officer	Ranch Hand	307	1.0173	0.0000 (-0.0009,0.0009)	0.972
	Comparison	462	1.0173		
Enlisted Flyer	Ranch Hand	133	1.0175	-0.0014 (-0.0028,0.0000)	0.052
	Comparison	185	1.0189		
Enlisted Groundcrew	Ranch Hand	337	1.0197	0.0005 (-0.0003,0.0014)	0.224
	Comparison	527	1.0192		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*1.0189*	*0.0000 (-0.0005,0.0006)*	*0.932*
	Comparison	*1,174*	*1.0189*		
Officer	Ranch Hand	307	1.0182	0.0000 (-0.0008,0.0009)	0.920
	Comparison	462	1.0181		
Enlisted Flyer	Ranch Hand	133	1.0182	-0.0013 (-0.0027,0.0001)	0.065
	Comparison	185	1.0195		
Enlisted Groundcrew	Ranch Hand	337	1.0198	0.0005 (-0.0003,0.0014)	0.244
	Comparison	527	1.0193		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	140	1.0183	1.0184	0.006	0.0002 (0.0002)	0.409
Medium	143	1.0188	1.0189			
High	141	1.0192	1.0192			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	140	1.0191	0.057	-0.0002 (0.0003)	0.454
Medium	143	1.0189			
High	141	1.0188			

Table 17-10. Analysis of Urine Specific Gravity (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,174	1.0184	1.0184		
Background RH	352	1.0179	1.0180	-0.0004 (-0.0011,0.0004)	0.352
Low RH	211	1.0186	1.0185	0.0001 (-0.0008,0.0011)	0.778
High RH	213	1.0190	1.0189	0.0005 (-0.0004,0.0015)	0.245
Low plus High RH	424	1.0188	1.0187	0.0003 (-0.0004,0.0010)	0.341

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,174	1.0188		
Background RH	352	1.0189	0.0001 (-0.0006,0.0009)	0.782
Low RH	211	1.0191	0.0003 (-0.0006,0.0012)	0.544
High RH	213	1.0185	-0.0003 (-0.0012,0.0007)	0.575
Low plus High RH	424	1.0188	0.0000 (-0.0007,0.0007)	0.987

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean	R^2	Slope (Standard Error)	p-Value
Low	260	1.0178	0.006	0.0003 (0.0001)	0.033*
Medium	258	1.0183			
High	258	1.0191			

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

*: Statistically significant (0.010<p-value≤0.050).

Table 17-10. Analysis of Urine Specific Gravity (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	260	1.0188	0.047	0.0000 (0.0002)	0.807
Medium	258	1.0190			
High	258	1.0186			

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

17.2.2.2.7 Urinary Occult Blood

The unadjusted and adjusted analyses revealed no significant differences in the percentage of urinary occult blood abnormalities for Models 1 through 4 (Table 17-11(a-h): p>0.06 for each analysis).

Table 17-11. Analysis of Urinary Occult Blood

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	***Ranch Hand***	***777***	***22 (2.8)***	***1.34 (0.75,2.39)***	***0.326***
	Comparison	***1,174***	***25 (2.1)***		
Officer	Ranch Hand	307	13 (4.2)	2.23 (0.94,5.27)	0.069
	Comparison	462	9 (1.9)		
Enlisted Flyer	Ranch Hand	133	2 (1.5)	0.93 (0.15,5.62)	0.934
	Comparison	185	3 (1.6)		
Enlisted Groundcrew	Ranch Hand	337	7 (2.1)	0.84 (0.33,2.12)	0.711
	Comparison	527	13 (2.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	***1,951***	***1.36 (0.76,2.43)***	***0.308***
Officer	769	2.20 (0.93,5.22)	0.073
Enlisted Flyer	318	0.92 (0.15,5.59)	0.925
Enlisted Groundcrew	864	0.87 (0.34,2.20)	0.761

Table 17-11. Analysis of Urinary Occult Blood (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	5 (3.6)	0.72 (0.45,1.16)	0.157
Medium	143	5 (3.5)		
High	141	3 (2.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
424	1.00 (0.56,1.78)	0.995

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	25 (2.1)		
Background RH	352	9 (2.6)	1.26 (0.58,2.75)	0.555
Low RH	211	9 (4.3)	2.02 (0.93,4.39)	0.077
High RH	213	4 (1.9)	0.84 (0.29,2.46)	0.755
Low plus High RH	424	13 (3.1)	1.30 (0.63,2.67)	0.473

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 17-11. Analysis of Urinary Occult Blood (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,174		
Background RH	352	1.20 (0.54,2.65)	0.654
Low RH	211	1.92 (0.88,4.20)	0.104
High RH	213	1.02 (0.34,3.09)	0.968
Low plus High RH	424	1.40 (0.67,2.91)	0.369

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	5 (1.9)	0.92 (0.71,1.21)	0.561
Medium	258	12 (4.7)		
High	258	5 (1.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
776	1.04 (0.74,1.46)	0.834

[a]Relative risk for a twofold increase in 1987 dioxin.

17.2.2.2.8 Urinary WBC Count

All unadjusted and adjusted analyses of urinary WBC count were nonsignificant for Models 1 through 4 (Table 17-12(a-h): p>0.08 for each analysis).

Table 17-12. Analysis of Urinary WBC Count

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*777*	*55 (7.1)*	*1.30 (0.90,1.88)*	*0.168*
	Comparison	*1,174*	*65 (5.5)*		
Officer	Ranch Hand	307	18 (5.9)	1.14 (0.61,2.13)	0.690
	Comparison	462	24 (5.2)		
Enlisted Flyer	Ranch Hand	133	7 (5.3)	1.41 (0.48,4.13)	0.528
	Comparison	185	7 (3.8)		
Enlisted Groundcrew	Ranch Hand	337	30 (8.9)	1.42 (0.85,2.36)	0.182
	Comparison	527	34 (6.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,951*	*1.32 (0.91,1.92)*	*0.145*
Officer	769	1.11 (0.59,2.08)	0.748
Enlisted Flyer	318	1.40 (0.48,4.12)	0.538
Enlisted Groundcrew	864	1.47 (0.88,2.46)	0.143

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	12 (8.6)	0.95 (0.73,1.24)	0.699
Medium	143	10 (7.0)		
High	141	12 (8.5)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
424	1.07 (0.78,1.46)	0.681

[a]Relative risk for a twofold increase in initial dioxin.

Table 17-12. Analysis of Urinary WBC Count (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	65 (5.5)		
Background RH	352	21 (6.0)	1.12 (0.67,1.86)	0.667
Low RH	211	18 (8.5)	1.58 (0.91,2.72)	0.102
High RH	213	16 (7.5)	1.35 (0.76,2.38)	0.306
Low plus High RH	424	34 (8.0)	1.46 (0.94,2.24)	0.089

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,174		
Background RH	352	1.17 (0.69,1.97)	0.559
Low RH	211	1.52 (0.88,2.64)	0.134
High RH	213	1.38 (0.76,2.50)	0.286
Low plus High RH	424	1.45 (0.93,2.25)	0.098

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	15 (5.8)	1.04 (0.88,1.23)	0.677
Medium	258	22 (8.5)		
High	258	18 (7.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 17-12. Analysis of Urinary WBC Count (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
776	0.97 (0.80,1.17)	0.735

[a]Relative risk for a twofold increase in 1987 dioxin.

17.2.2.2.9 Urinary Protein

All unadjusted and adjusted analyses of urinary protein were nonsignificant for Models 1 through 4 (Table 17-13(a-h): p>0.18 for each analysis).

Table 17-13. Analysis of Urinary Protein

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Number (%) Present**	**Unadjusted Relative Risk (95% C.I.)**	**p-Value**
All	*Ranch Hand*	*777*	*26 (3.3)*	*0.79 (0.49,1.29)*	*0.348*
	Comparison	*1,174*	*49 (4.2)*		
Officer	Ranch Hand	307	7 (2.3)	0.75 (0.30,1.87)	0.533
	Comparison	462	14 (3.0)		
Enlisted Flyer	Ranch Hand	133	5 (3.8)	0.99 (0.31,3.20)	0.991
	Comparison	185	7 (3.8)		
Enlisted Groundcrew	Ranch Hand	337	14 (4.2)	0.77 (0.40,1.49)	0.441
	Comparison	527	28 (5.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED			
Occupational Category	**n**	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	*1,951*	*0.81 (0.50,1.34)*	*0.416*
Officer	769	0.73 (0.29,1.86)	0.513
Enlisted Flyer	318	0.98 (0.30,3.23)	0.978
Enlisted Groundcrew	864	0.82 (0.42,1.59)	0.549

Table 17-13. Analysis of Urinary Protein (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	5 (3.6)	0.98 (0.67,1.43)	0.901
Medium	143	4 (2.8)		
High	141	6 (4.3)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
424	0.88 (0.57,1.37)	0.566

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with urinary protein present.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	49 (4.2)		
Background RH	352	11 (3.1)	0.90 (0.46,1.76)	0.754
Low RH	211	7 (3.3)	0.70 (0.31,1.60)	0.401
High RH	213	8 (3.8)	0.74 (0.34,1.61)	0.443
Low plus High RH	424	15 (3.5)	0.72 (0.39,1.32)	0.287

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 17-13. Analysis of Urinary Protein (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,174		
Background RH	352	1.12 (0.56,2.26)	0.748
Low RH	211	0.64 (0.28,1.48)	0.299
High RH	213	0.68 (0.31,1.52)	0.351
Low plus High RH	424	0.66 (0.36,1.22)	0.188

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	4 (1.5)	1.12 (0.88,1.42)	0.347
Medium	258	12 (4.7)		
High	258	10 (3.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
776	0.98 (0.74,1.29)	0.863

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with urinary protein present.

17.3 DISCUSSION

The AFHS evaluated renal (kidney) disorders based on the medical histories and laboratory measures. The clinical histories and laboratory values were measured in accordance with the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines recently established by the National Kidney Foundation (57). The Foundation published the guidelines to assist clinicians in evaluating, classifying, and stratifying persons with chronic kidney disease.

The K/DOQI guidelines stress the importance of assessing the glomerular filtration rate (GFR) and urinary composition (albuminuria, proteinuria, abnormal cells) of an individual to determine the presence of kidney disease. The AFHS assessed the GFR using standard laboratory measures recommended by the K/DOQI, including the serum creatinine test and the Cockroft-Gault (52-54) equation, which estimates creatinine clearance based on age, weight, and gender. A person with a low GFR is at a higher risk of progressive loss of kidney function and complications due to kidney disease (e.g., uremia, anemia, metabolic bone disease) than a person with a high GFR. The AFHS assessment of urinary composition also was consistent with the guidelines, focusing on the presence of albuminuria, proteinuria, and formed elements (RBCs and WBCs) in the urine. The use of the urinary albumin or protein-to-creatinine ratio as an index of total albumin or protein excretion has been approved and adopted by the K/DOQI as the screening measure of choice, particularly when validating diabetic nephropathy.

The AFHS cutpoints for hematuria and pyuria (two cells per HPF) will miss few cases of disease, but may cause inclusion of more healthy subjects than would a higher cutpoint. Abnormalities based on the AFHS cutpoints are considered a minor abnormality, which are not always a sign of renal parenchymal disease, and will frequently resolve spontaneously without the need for an indepth evaluation. Other measures, such as the urine specific gravity and the blood urea nitrogen, were of lesser value in the assessment of kidney disease than the other parameters studied in this evaluation. The assessment of kidney stones relied largely on clinical history, which, considering the pain associated with this common disorder, was judged to be a reliable measure. In addition, if the AFHS had used plain films, the films would have not picked up passed stones and would have identified only roughly 85 percent of stones if they were present (i.e., approximately 15 percent are radiolucent).

In the dependent variable-covariate associations, the findings were in complete agreement with established clinical patterns regarding kidney stones and kidney function. With respect to kidney stones, there was an increase with age and greater prevalence in non-Blacks versus Blacks. Regarding kidney disease, there was an increase in prevalence with age, Blacks, and diabetics. This was reflected both in the parameters of GFR and in the incidence of proteinuria, albuminuria, and abnormal urine sediment. Age, race, and diabetic class were significantly associated with the majority of the renal parameters studied. The adjusted analysis took into account age, race, military occupation, and diabetic status. Analysis of albuminuria was also adjusted for the participants' use of various anti-hypertensive agents.

Several models were used in the 2002 AFHS evaluation to assess renal function in participants exposed to herbicides or dioxin. Model 1 evaluated Ranch Hands to a matched Comparison group, whereas the other models (Models 2, 3, and 4) assessed dose-response effects using three alternative measures of serum dioxin. Given the number of measurements and contrasts, it would be prudent to interpret with caution any significant finding not supported by other significant findings. To judge whether herbicide or dioxin exposure is linked to any one abnormality, it would be ideal to see the effect in all models in a dose-dependent fashion. That is, a story should emerge from data analysis with some internal consistency.

There was no difference in Ranch Hands and Comparisons in the adjusted analysis of kidney stones. In the models involving dioxin exposure, there was no evidence of increased risk with dioxin exposure; in fact, the models suggested a decreased risk with increasing dioxin exposure. No significant findings of

increased risk with herbicide or dioxin exposure existed in the analyses of kidney disease or blood urea nitrogen after adjusting for age, race, military occupation, and diabetic class.

Serum creatinine and creatinine clearance were the laboratory measures used to assess GFR. Mean values of serum creatinine were significantly lower in Ranch Hands relative to Comparisons and the adjusted analyses in the models using dioxin levels were not significant. These findings suggest a higher GFR in Ranch Hands. Serum creatinine, however, is affected not only by GFR, but also by muscle mass, meat intake, and the secretion of creatinine into urine (creatinine enters urine by glomerular filtration and secretion). An effect on GFR is also not supported by the creatinine clearance analysis, which shows that Ranch Hands and Comparisons were no different in the adjusted analyses. The models using categorized dioxin and 1987 levels of dioxin actually suggest a higher GFR in persons with the greatest exposures. These findings would not be expected if increasing levels of dioxin were doing harm to the renal system, as individuals with a low GFR are at higher risk of progressive loss of kidney function and complications due to kidney disease.

Ranch Hands had significantly lower albuminuria than Comparisons in the adjusted analyses. In Model 3, Ranch Hands in the low and high dioxin categories combined had significantly lower albuminuria than Comparisons. Models using initial dioxin exposure or 1987 dioxin levels did not support this dioxin association. Lower excretion of albumin in the urine is not a marker of any known kidney disease in clinical practice.

The prevalences of microhematuria, pyuria, and proteinuria were similar in Ranch Hands and Comparisons. There was no apparent association with herbicide or dioxin exposure on these urinalysis results.

17.4 SUMMARY

The renal assessment was based on questionnaire data, which was subsequently verified by a review of medical records, and laboratory data. Associations with herbicide exposure (i.e., group – Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable in the renal assessment. The significant adjusted results are discussed in the sections below.

17.4.1 Model 1: Group Analysis

Adjusted group analyses revealed that Ranch Hands had a significantly lower mean serum creatinine level than Comparisons, as well as a lower mean urinary microalbumin to urinary creatinine ratio than Comparisons. Stratifying by military occupation revealed Ranch Hand officers had a significantly lower mean serum creatinine level than Comparison officers. In addition, among enlisted groundcrew, Ranch Hands had a significantly lower mean urinary microalbumin to urinary creatinine ratio than Comparisons. The results of all unadjusted and adjusted Model 1 analyses are summarized in Table 17-14.

Table 17-14. Summary of Group Analysis (Model 1) for Renal Variables (Ranch Hands vs. Comparisons)

| | UNADJUSTED | | | |
| | | | | |
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Occurrence of Kidney Stones (D)	NS	NS	ns	ns
Occurrence of Past Kidney Disease (D)	ns	ns	NS	ns
Laboratory				
Blood Urea Nitrogen (C)	ns	ns	ns	ns
Serum Creatinine (C)	p=0.038 (-0.02)	p=0.025 (-0.03)	NS	ns
Creatinine Clearance (C)[a]	NS	NS	ns	NS
Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero Measurements) (C)	p=0.008 (-11.93)	NS	ns	p=0.002 (-17.48)
Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero versus Zero) (D)	NS	NS	NS	NS
Urine Specific Gravity (C)	NS	NS	ns	NS
Urinary Occult Blood (D)	NS	NS	ns	ns
Urinary WBC Count (D)	NS	NS	NS	NS
Urinary Protein (D)	ns	ns	ns	ns

[a] A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: NS or ns: Not significant (p>0.05).
   C: Continuous form of dependent variable.
   D: Discrete form of dependent variable.

   The p-value was given if p≤0.05. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

   A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

| | ADJUSTED | | | |
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Occurrence of Kidney Stones (D)	NS	NS	ns	ns
Occurrence of Past Kidney Disease (D)	ns	ns	NS	ns
Laboratory				
Blood Urea Nitrogen (C)	ns	ns	ns	ns
Serum Creatinine (C)	p=0.031 (-0.02)	p=0.010 (-0.04)	NS	ns
Creatinine Clearance (C)[a]	NS	NS	ns	NS
Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero Measurements) (C)	p=0.037 (-12.69)	NS	ns	p=0.024 (-19.06)
Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero versus Zero) (D)	NS	NS	NS	NS
Urine Specific Gravity (C)	NS	NS	ns	NS
Urinary Occult Blood (D)	NS	NS	ns	ns
Urinary WBC Count (D)	NS	NS	NS	NS
Urinary Protein (D)	ns	ns	ns	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: NS or ns: Not significant (p>0.05).
　　　C: Continuous form of dependent variable.
　　　D: Discrete form of dependent variable.

　　　The p-value was given if p≤0.05. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

　　　A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

17.4.2 Model 2: Initial Dioxin Analysis

After adjusting for covariates, the Model 2 analysis revealed no significant relations with initial dioxin. The results of all unadjusted and adjusted Model 2 analyses are summarized in Table 17-15.

Table 17-15. Summary of Initial Dioxin Analysis (Model 2) for Renal Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Occurrence of Kidney Stones (D)	p=0.008 (0.72)	ns
Occurrence of Past Kidney Disease (D)	NS	NS
Laboratory		
Blood Urea Nitrogen (C)	ns	NS
Serum Creatinine (C)	p=0.010 (-0.016)	ns
Creatinine Clearance (C)[a]	p=0.001 (0.132)	ns
Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero Measurements) (C)	NS	NS
Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero versus Zero) (D)	ns	ns
Urine Specific Gravity (C)	NS	ns
Urinary Occult Blood (D)	ns	NS
Urinary WBC Count (D)	ns	NS
Urinary Protein (D)	ns	ns

[a]A negative slope was considered adverse for this variable.

Note: NS or ns: Not significant (p>0.05).
   C: Continuous form of dependent variable.
   D: Discrete form of dependent variable.

   The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

   A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

17.4.3   Model 3: Categorized Dioxin Analysis

The adjusted Model 3 analysis revealed significantly lower mean creatinine clearance values among Comparisons than among Ranch Hands in the low dioxin category. In addition, Comparisons displayed a significantly lower mean creatinine clearance value than the Ranch Hands in the combined low and high dioxin categories. The mean urinary microalbumin to urinary creatinine ratio was significantly lower for Ranch Hands in the low dioxin category than for Comparisons. The results of all unadjusted and adjusted Model 3 analyses are summarized in Table 17-16.

Table 17-16. Summary of Categorized Dioxin Analysis (Model 3) for Renal Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Medical Records				
Occurrence of Kidney Stones (D)	NS	p=0.033 (1.58)	ns	NS
Occurrence of Past Kidney Disease (D)	ns	ns	ns	ns
Laboratory				
Blood Urea Nitrogen (C)	ns	ns	p=0.044 (-0.70)	ns
Serum Creatinine (C)	ns	NS	p=0.003 (-0.05)	ns
Creatinine Clearance (C)[a]	ns	NS	p<0.001 (7.06)	p=0.003 (3.56)
Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero Measurements) (C)	ns	p=0.039 (-12.49)	ns	p=0.024 (-11.26)
Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero versus Zero) (D)	NS	NS	NS	NS
Urine Specific Gravity (C)	ns	NS	NS	NS
Urinary Occult Blood (D)	NS	NS	ns	NS
Urinary WBC Count (D)	NS	NS	NS	NS
Urinary Protein (D)	ns	ns	ns	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: NS or ns: Not significant (p>0.05).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

	ADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Medical Records				
Occurrence of Kidney Stones (D)	ns	NS	ns	NS
Occurrence of Past Kidney Disease (D)	ns	ns	ns	ns
Laboratory				
Blood Urea Nitrogen (C)	ns	ns	ns	ns
Serum Creatinine (C)	ns	ns	ns	ns
Creatinine Clearance (C)[a]	NS	p=0.015 (2.92)	NS	p=0.014 (2.26)
Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero Measurements) (C)	ns	p=0.033 (-16.47)	ns	ns
Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero versus Zero) (D)	NS	NS	ns	NS
Urine Specific Gravity (C)	NS	NS	ns	NS
Urinary Occult Blood (D)	NS	NS	NS	NS
Urinary WBC Count (D)	NS	NS	NS	NS
Urinary Protein (D)	NS	ns	ns	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: NS or ns: Not significant (p>0.05).
    C: Continuous form of dependent variable.
    D: Discrete form of dependent variable.

    The p-value was given if p≤0.05. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

    A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

17.4.4 Model 4: 1987 Dioxin Level Analysis

Model 4 analyses showed a significant increase in adjusted mean creatinine clearance values as 1987 dioxin levels increased. All results for Model 4 unadjusted and adjusted analyses are summarized in Table 17-17.

Table 17-17. Summary of 1987 Dioxin Analysis (Model 4) for Renal Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Occurrence of Kidney Stones (D)	ns	ns
Occurrence of Past Kidney Disease (D)	NS	NS
Laboratory		
Blood Urea Nitrogen (C)	ns	NS
Serum Creatinine (C)	ns	ns
Creatinine Clearance (C)[a]	p<0.001 (0.173)	p<0.001 (0.118)
Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero Measurements) (C)	NS	NS
Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero versus Zero) (D)	NS	ns
Urine Specific Gravity (C)	p=0.033 (0.0003)	NS
Urinary Occult Blood (D)	ns	NS
Urinary WBC Count (D)	NS	ns
Urinary Protein (D)	NS	ns

[a] A negative slope was considered adverse for this variable.

Note: NS or ns: Not significant (p>0.05).
        C: Continuous form of dependent variable.
        D: Discrete form of dependent variable.

        The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

        A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

17.4.5   Summary of Significant Results

Table 17-18 summarizes the significant results (p≤0.05) for the adjusted analyses that were performed for the renal assessment. The dependent variable and its table reference are listed along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and is explained in footnotes.

Table 17-18. Summary of Results from Significant Adjusted Analyses in the Renal Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Serum Creatinine (17-6)	1	RH vs. C, All	0.031	-0.02	RH: 1.17 mg/dL C: 1.19 mg/dL	(a)
	1	RH vs. C, Officer	0.010	-0.04	RH: 1.16 mg/dL C: 1.20 mg/dL	(a)
Creatinine Clearance (17-7)	3	Low RH vs. C	0.015	2.92	RH: 85.27 C: 82.35	(b)
	3	Low plus High RH vs. C	0.014	2.26	RH: 84.61 C: 82.35	(b)
	4	All RH: 1987 Dioxin	<0.001	0.118 (0.025)	Low: 79.36 Medium: 85.48 High: 86.92	(c)
Urinary Microalbumin to Urinary Creatinine Ratio (17-8)	1	RH vs. C, All	0.037	-12.69	RH: 27.44 μg/mg C: 40.13 μg/mg	(a)
	1	RH vs. C, Enlisted Groundcrew	0.024	-19.06	RH: 23.85 μg/mg C: 42.91 μg/mg	(a)
	3	Low RH vs. C	0.033	-16.47	RH: 22.00 μg/mg C: 38.47 μg/mg	(b)

(a): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were transformed to original scale and were presented for each exposure group in contrast.

(b): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were transformed to original scale and were presented for each dioxin category in contrast.

(c): Continuous variable: slope and standard error were presented and were based on square root of dependent variable versus $\log_2$ (1987 dioxin); adjusted means were transformed to original scale and were presented for each of three 1987 dioxin categories.

Note: RH = Ranch Hand.
        C = Comparison.

  Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
             Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
             High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

  Model 4:   Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

17.5   CONCLUSION

One of the goals of the AFHS was to determine whether herbicide or dioxin exposure increases the risk of renal disease. Evaluating the presence or absence of kidney disease among participants was done through the study of clinical histories and laboratory parameters. The study applied screening parameters used today in clinical practice to determine the presence of disease.

Ranch Hands had a lower mean serum creatinine level, as well as a lower mean urinary microalbumin to urinary creatinine ratio. The mean urinary microalbumin to urinary creatinine ratio was higher for Comparisons than for Ranch Hands in the low dioxin category. Lower mean creatinine clearance values

were observed more often among Comparisons than among Ranch Hands in the low dioxin category. An increase in mean creatinine clearance values was observed as 1987 dioxin levels increased.

The results from the renal assessment indicated no association between any marker of kidney disease and either herbicides or dioxin. In particular, there was no evidence that exposure to herbicides or dioxin was associated with renal dysfunction, kidney stones, reduction in glomerular filtration rate, incidence of proteinuria or albuminuria, or cells in the urine.

REFERENCES

1. Bernard, A.M. 2001. Clinical Renal Toxicology. In: Clinical Environmental Health and Toxic Exposures. J.B.J. Sullivan, and G.R. Krieger, eds. 2nd ed. Lippincott Williams & Wilkins: Tucson, AZ.

2. Erne, K. 1966. Studies on the animal metabolism of phenoxyacetic herbicides. *Acta Veterinaria Scandinavica* 7:264-71.

3. Kohli, J.D., R.N. Khanna, B.N. Gupta, M.M. Dhar, J.S. Tandon, and K.P. Sircar. 1974. Absorption and excretion of 2,4,5-trichlorophenoxyacetic in man. *Archives internationales de pharmacodynamie et de therapie* 210:250-5.

4. Gehring, P.J., C.G. Kramer, B.A. Schwetz, J.Q. Rose, and V.K. Rowe. 1973. The fate of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) following oral administration to man. *Toxicology and Applied Pharmacology* 26:352-61.

5. Olson, J.R. 1986. Metabolism and disposition of 2,3,7,8-tetrachlorodibenzo-p-dioxin in guinea pigs. *Toxicology and Applied Pharmacology* 85:263-73.

6. Poiger, H., and C. Schlatter. 1986. Pharmacokinetics of 2,3,7,8-TCDD in man. *Chemosphere* 15:1489-94.

7. Lilienfeld, D.E., and M.A. Gallo. 1989. 2,4-D, 2,4,5-T, and 2,3,7,8-TCDD: An overview. *Epidemiologic Reviews* 11:28-58.

8. U.S. Environmental Protection Agency. 1984. Health assessment document for polychlorinated dibenzo-p-dioxins. Cincinnati, OH.

9. DeCaprio, A.P., D.N. McMartin, P.W. O'Keefe, R. Rej, J.B. Silkworth, and L.S. Kaminsky. 1986. Subchronic oral toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the guinea pig: Comparisons with a PCB-containing transformer fluid pyrolysate. *Fundamental and Applied Toxicology* 6:454-63.

10. Silkworth, J.B., D.S. Cutler, L. Antrim, D. Houston, C. Tumasonis, and L.S. Kaminsky. 1989. Teratology of 2,3,7,8-tetrachlorodibenzo-p-dioxin in a complex environmental mixture from the Love Canal. *Fundamental and Applied Toxicology* 13:1-15.

11. Birnbaum, L.S., M.W. Harris, L.M. Stocking, A.M. Clark, and R.E. Morrissey. 1989. Retinoic acid and 2,3,7,8-tetrachlorodibenzo-p-dioxin selectively enhance teratogenesis in C57BL/6N mice. *Toxicology and Applied Pharmacology* 98:487-500.

12. Couture, L.A., M.W. Harris, and L.S. Birnbaum. 1989. Characterization of TCDD-induced hydronephrosis relative to cleft palate in C57BL/6N mice. *Toxicologist* 9:117.

13. Olson, J.R., and B.P. McGarrigle. 1989. Fetal toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the rat and hamster. *Toxicologist* 9:117.

14. Bowes, R.C., and K.S. Ramos. 1994. Assessment of cell-specific cytotoxic responses of the kidney to selected aromatic hydrocarbons. *Toxicology in Vitro* 8:1151-60.

15. Parrish, A.R., N.F. Alejandro, R.C. Bowes, and K.S. Ramos. 1998. Cytotoxic response profiles of cultured renal epithelial and mesenchymal cells to selected aromatic hydrocarbons. *Toxicology in Vitro* 12:219-32.

16. Slezak, B.P., G.E. Hatch, M.J. DeVito, J.J. Diliberto, R. Slade, K. Crissman, E. Hassoun, and L.S. Birnbaum. 2000. Oxidative stress in female B6C3F1 mice following acute and subchronic exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicological Sciences* 54:390-8.

17. Kraemer, S.A., K.A. Arthur, M.S. Denison, W.L. Smith, and D.L. DeWitt. 1996. Regulation of prostaglandin endoperoxide H synthase-2 expression by 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Archives of Biochemistry and Biophysics* 330:319-28.

18. Institute of Medicine. 2001. Veterans and Agent Orange: Update 2000. National Academy Press: Washington, DC.

19. Carter, C.D., R.D. Kimbrough, J.A. Liddle, R.E. Cline, M.M. Zack, W.F. Barthel, R.E. Koehler, and P.E. Phillips. 1975. Tetrachlorodibenzodioxin: An accidental poisoning episode in horse arenas. *Science* 188:738-40.

20. Merlo, F., ed. 1985. Adverse health effects in human population exposed to 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD) in Seveso: An update. Hemisphere Publishing Corporation: Washington, DC.

21. Bertazzi, P.A. 1991. Long-term effects of chemical disasters. Lessons and results from Seveso. *The Science of the Total Environment* 106:5-20.

22. Hoffman, R.E., P.A. Stehr-Green, K.B. Webb, R.G. Evans, A.P. Knutsen, W.F. Schramm, J.L. Staake, B.B. Gibson, and K.K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *The Journal of the American Medical Association* 255:2031-8.

23. Mocarelli, P., L.L. Needham, A. Marocchi, D.G. Patterson, Jr., P. Brambilla, P.M. Gerthoux, L. Meazza, and V. Carreri. 1991. Serum concentrations of 2,3,7,8-tetrachlorodibenzo-p-dioxin and test results from selected residents of Seveso, Italy. *Journal of Toxicology and Environmental Health* 32:357-66.

24. Pesatori, A.C., C. Zocchetti, S. Guercilena, D. Consonni, D. Turrini, and P.A. Bertazzi. 1998. Dioxin exposure and non-malignant health effects: A mortality study. *Occupational and Environmental Medicine* 55:126-31.

25. Bertazzi, P.A., I. Bernucci, G. Brambilla, D. Consonni, and A.C. Pesatori. 1998. The Seveso studies on early and long-term effects of dioxin exposure: A review. *Environmental Health Perspectives* 106(Suppl 2):625-33.

26. Bertazzi, P.A., D. Consonni, S. Bachetti, M. Rubagotti, A. Baccarelli, C. Zocchetti, and A.C. Pesatori. 2001. Health effects of dioxin exposure: A 20-year mortality study. *American Journal of Epidemiology* 153:1031-44.

27. Webb, K., R.G. Evans, P. Stehr, and S.M. Ayres. 1987. Pilot study on health effects of environmental 2,3,7,8-TCDD in Missouri. *American Journal of Industrial Medicine* 11:685-91.

28. Stehr-Green, P.A., R.E. Hoffman, K. Webb, R.G. Evans, A.P. Knutsen, W. Schramm, J.L. Staake, B.B. Gibson, and K.K. Steinberg. 1987. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Chemosphere* 16:2089-94.

29. Cook, R.R., G.G. Bond, R.A. Olson, and M.G. Ott. 1987. Update of the mortality experience of workers exposed to chlorinated dioxins. *Chemosphere* 16:2111-6.

30. Collins, J.J., M.E. Strauss, G.J. Levinskas, and P.R. Conner. 1993. The mortality experience of workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin in a trichlorophenol process accident. *Epidemiology* 4:7-13.

31. Ott, M.G., and A. Zober. 1996. Cause specific mortality and cancer incidence among employees exposed to 2,3,7,8-TCDD after a 1953 reactor accident. *Occupational and Environmental Medicine* 53:606-12.

32. Hooiveld, M., D.J. Heederik, M. Kogevinas, P. Boffetta, L.L. Needham, D.G. Patterson, Jr., and H.B. Bueno-de-Mesquita. 1998. Second follow-up of a Dutch cohort occupationally exposed to phenoxy herbicides, chlorophenols, and contaminants. *American Journal of Epidemiology* 147:891-901.

33. Vena, J., P. Boffetta, H. Becher, T. Benn, H.B. Bueno-de-Mesquita, D. Coggon, D. Colin, D. Flesch-Janys, L. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, N. Pearce, A.C. Pesatori, R. Saracci, K. Steenland, and M. Kogevinas. 1998. Exposure to dioxin and nonneoplastic mortality in the expanded IARC international cohort study of phenoxy herbicide and chlorophenol production workers and sprayers. *Environmental Health Perspectives* 106(Suppl 2):645-53.

34. Suskind, R.R., and V.S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *The Journal of the American Medical Association* 251:2372-80.

35. Zober, A., M.G. Ott, and P. Messerer. 1994. Morbidity follow up study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

36. Neuberger, M., C. Rappe, S. Bergek, H. Cai, M. Hansson, R. Jager, M. Kundi, C.K. Lim, H. Wingfors, and A.G. Smith. 1999. Persistent health effects of dioxin contamination in herbicide production. *Environmental Research* 81:206-14.

37. Stellman, S.D., J.M. Stellman, and J.F. Sommer, Jr. 1988. Health and reproductive outcomes among American Legionnaires in relation to combat and herbicide exposure in Vietnam. *Environmental Research* 47:150-74.

38. U.S. Centers for Disease Control. 1988. Health status of Vietnam veterans. II. Physical health. The Centers for Disease Control Vietnam Experience Study. *The Journal of the American Medical Association* 259:2708-14.

39. Crane, P.J., D.L. Barnard, K.D. Horsley, and M.A. Adena. 1997. Mortality of Vietnam veterans: The veteran cohort study: A report of the 1996 retrospective cohort study of Australian Vietnam veterans. Department of Veterans Affairs: Canberra.

40. Dalager, N.A., and H.K. Kang. 1997. Mortality among Army Chemical Corps Vietnam veterans. *American Journal of Industrial Medicine* 31:719-26.

41. Thomas, T.L., and H.K. Kang. 1990. Mortality and morbidity among Army Chemical Corps Vietnam veterans: A preliminary report. *American Journal of Industrial Medicine* 18:665-73.

42. Bullman, T.A., and H.K. Kang. 1996. The risk of suicide among wounded Vietnam veterans. *American Journal of Public Health* 86:662-7.

43. Michalek, J.E., N.S. Ketchum, and F.Z. Akhtar. 1998. Postservice mortality of US Air Force veterans occupationally exposed to herbicides in Vietnam: 15-year follow-up. *American Journal of Epidemiology* 148:786-92.

44. Wolfe, W.H., J.E. Michalek, J.C. Miner, A. Rahe, J. Silva, W.F. Thomas, W.D. Grubbs, M.B. Lustik, T.G. Karrison, R.H. Roegner, and D.E. Williams. 1990. Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. I. Physical health. *The Journal of the American Medical Association* 264:1824-31.

45. Roegner, R.H., W.D. Grubbs, M.B. Lustik, A.S. Brockman, S.C. Henderson, D.E. Williams, W.H. Wolfe, J.E. Michalek, and J.C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

46. Grubbs, W.D., W.H. Wolfe, J.E. Michalek, D.E. Williams, M.B. Lustik, A.S. Brockman, S.C. Henderson, F.R. Burnett, R.G. Land, D.J. Osborne, V.K. Rocconi, M.E. Schreiber, J.C. Miner, G.L. Henriksen, and J.A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1992 followup examination results. NTIS: AD A 304 306, 304 308-316. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

47. Sweeney, M.H., and P. Mocarelli. 2000. Human health effects after exposure to 2,3,7,8-TCDD. *Food Additives and Contaminants* 17:303-16.

48. Institute of Medicine. 1994. Health effects of herbicides used in Vietnam. National Academy Press: Washington, DC.

49. Institute of Medicine. 1997. Veterans and Agent Orange: Update 1996. National Academy Press: Washington, DC.

50. Institute of Medicine. 1999. Veterans and Agent Orange: Update 1998. National Academy Press: Washington, DC.

51. Institute of Medicine. 2003. Veterans and Agent Orange: Update 2002. National Academy Press: Washington, DC.

52. Coresh, J., R.D. Toto, K.A. Kirk, P.K. Whelton, S. Massry, C. Jones, L. Agodoa, and F. Van Lente. 1998. Creatinine clearance as a measure of glomerular filtration rate in screenees for the African-American study of kidney disease and hypertension pilot study. *American Journal of Kidney Diseases* 32(1):32-42.

53. Lam, N., R. Sperelakis, J. Kuk, J. Seeger, and A. Lau. 1999. Rapid estimation of creatinine clearance in patients with liver disease. *Digestive Diseases and Science* 44(6):1222-7.

54. Cockroft, D.W., and M. Gault. 1976. Prediction of creatinine clearance from serum creatinine. *Nephronology* 16(1):31-41.

55. Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L. R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

56. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57(6):369-78.

57. National Kidney Foundation. 2002. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification and stratification. *American Journal of Kidney Diseases* 39(Supplement 1):S1-S000.

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18 ENDOCRINOLOGY ASSESSMENT

18.1 INTRODUCTION

18.1.1 Background

18.1.1.1   Organs/Diseases

Several sites of endocrine activity, including the thyroid gland, pancreas, and hypothalamic-pituitary-testis axis have been evaluated for dioxin toxicity in animal and human studies. Ranch Hands and Comparisons were evaluated for thyroid disease, diabetes, and testosterone and other sex hormone levels as part of the endocrinology assessment in the Air Force Health Study (AFHS).

The thyroid produces thyroxine (T_4) and triiodothyronine (T_3), hormones that are released in response to thyroid-stimulating hormone (TSH) secreted by the anterior pituitary gland. To maintain thyroid hormone homeostasis, the pituitary is stimulated to release more TSH when circulating T_3 and T_4 levels are low. Conversely, high levels of circulating T_3 and T_4 trigger the pituitary to reduce TSH production. Disruptions in this feedback loop can lead to diseases such as hypothyroidism and hyperthyroidism. A family history of thyroid disease and age are positively associated with both hypothyroidism and hyperthyroidism.

The two most important hormones secreted by the pancreas are insulin and glucagon. Insulin stimulates liver cells to take up glucose from the blood and convert it into glycogen. Glucagon stimulates the conversion of glycogen into glucose, which is then released into the blood. The production of insulin is regulated by blood glucose concentrations; high blood glucose concentrations combined with insulin deficiency results in diabetes. Type 1 diabetes is a condition caused by a genetically based autoimmune destruction of β-cells and the subsequent inability of the body to manufacture insulin (1). Type 2 diabetes, the diagnosis given to approximately 90 percent of all diabetes cases, describes a combination of insulin resistance, insulin deficiency, and glucose overproduction. Risk factors for Type 2 diabetes include older age and being overweight and physically inactive. Additional risk factors for diabetes include a family history of diabetes, ethnicity, abnormal blood lipid levels, and high blood pressure (2, 3).

The hypothalamic-pituitary-testis axis produces several hormones affecting gonadal function. The hypothalamus releases gonadotropin-releasing hormone that subsequently signals the pituitary to release luteinizing hormone (LH), the hormone that regulates growth and development of eggs and sperm. Within the testis, LH stimulates testosterone production in the Leydig cells. Testosterone from the testes, as well as follicle-stimulating hormone (FSH) released by the pituitary, stimulates production of sperm. Excess testosterone converts to estradiol by the aromatase enzyme. Male-mediated adverse reproductive effects can be due to any number of imbalances in gonadal hormones produced via the hypothalamic-pituitary-testis axis. Although not analyzed in this report, the AFHS examined outcomes such as sex of offspring, pre-term birth, intrauterine growth retardation, and infant deaths (4, 5), all of which are discussed further in this section.

18.1.1.2   Toxicology

Dioxin binds to the aryl hydrocarbon (Ah) receptor, which has similarities to the endocrine receptors that mediate function of the thyroid, adrenal, and gonadal hormones (6-9). Animal research documented that the thyroid is a target organ for dioxin toxicity, although the mechanism has not been defined clearly and

remains under investigation (10-17). Also, dioxin-induced changes in thyroid indices (T_4, T_3, and TSH) differ according to species and strain specificity (18, 19), as well as dose and duration of exposure (20, 21).

Studies of guinea pigs, rats, and mice that have been dosed with dioxin at levels between 0.03 – 1.0 μg per kg demonstrated reduced glucose transport activity in adipose, liver, and pancreas tissue (22-26). Glucose and insulin levels decreased in rats dosed with dioxin in excess of 100 mg per kg (27, 28). The mechanism by which dioxin alters glucose transport remains unknown.

Additional experiments explored the effects of dioxin on the pituitary and hypothalamus (29, 30). The use of microsurgical techniques in male rats revealed that removal of the pituitary gland aggravated dioxin toxicity, but the effect was attenuated upon administering either corticosterone or thyroid hormone (29). Another study defined a biochemical basis for the effect of dioxin on prolactin levels controlled by the adenohypophysis in male rats (31). Studies on the effects of dioxin on the pituitary-adrenal axis documented significant suppression of corticosterone production by the adrenal gland (32) and defined a biochemical basis for the apparent reduction in bioactivity of adrenocorticotropic hormone secreted by the pituitary (33).

The finding in laboratory animals of physicochemical similarities between the dioxin-binding Ah and glucocorticoid receptors (9, 34) has prompted further investigation into the interaction of dioxin with other steroid hormones. Couture and colleagues (35) provided a comprehensive review of the research into the developmental toxicity and teratogenicity of dioxin in experimental animals.

Experimental studies documented numerous adverse male reproductive effects in laboratory animals exposed to dioxin, including reduced testicular weight, impaired spermatogenesis, decreased testicular testosterone secretion, and atrophy of the androgen-sensitive seminal vesicles and epididymis (36-43). Although dioxin administration is associated with diminished testosterone secretion in rats (39, 44, 45), the mechanism is unknown and may involve the hypothalamic-pituitary axis. In rats, dioxin inhibits the secretion of LH by the pituitary gland, an effect associated with androgen deficiency (46, 47). In other experiments, dioxin inhibited the response of the pituitary to gonadotropin-releasing hormone secreted by the hypothalamus (48).

18.1.1.3   Epidemiology: Thyroid Disease

Zober and colleagues (49) reported an increase in thyroid disease among workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin) following a 1953 industrial accident in a trichlorophenol production unit in Germany. Thyroid disease and goiter occurred more frequently among dioxin-exposed workers, including those with an occupational history of chloracne as an indicator of high exposure, than among referents. Thyrotoxicosis, or hyperthyroidism, and hypothyroidism were reported among a small number of workers with dioxin concentrations of at least 1,000 parts per trillion (ppt) and a history of moderate to severe chloracne. In the analyses of laboratory measurements from the same exposed population, the researchers found positive associations between each of the exposure indices and selected tests of thyroid function: T_4 and thyroxine binding globulin (50).

Workers at two plants that manufactured 2,4,5-T or one of its derivatives had a statistically significantly higher adjusted mean free T_4 index than referents and a higher adjusted mean total T_4 (51). Although the adjusted mean total T_4 and T_4 index were higher for workers in each category of exposure compared to referents, a dose-response trend was not observed. Adjusted mean TSH did not differ between workers and referents.

After adjusting for age, race, and military occupation, Pavuk and colleagues (52) found that Ranch Hands in the low and high dioxin categories had significantly higher TSH than the Comparison population, with a significant increase in TSH with increased exposure. No changes in clinical thyroid disease were seen.

In 2002, the Institute of Medicine (IOM) (53) concluded that there is inadequate or insufficient evidence to determine if an association existed between Agent Orange and other herbicides used in Vietnam and altered thyroid function.

18.1.1.4   Epidemiology: Diabetes

The possibility that dioxin might affect glucose metabolism in humans was first raised in 1981 with the publication of an occupational study that reported an unusually high prevalence of abnormal glucose tolerance tests (40%) and a 20-percent incidence of diabetes in chemical production workers exposed to dioxin (54). Since then, several studies examined the association between occupational dioxin exposure and diabetes or related indicators, including those conducted by the National Institute of Occupational Safety and Health (NIOSH) (51, 55, 56), the International Agency for Research on Cancer (57), and BASF (49, 50). Other studies examined this association among Seveso, Italy, residents (58) and Vietnam veterans (59-62).

A NIOSH study (56) reported statistically significant associations between the prevalence of diabetes and elevated fasting blood sugar with increasing serum dioxin levels among workers employed more than 15 years earlier at one of two plants that produced trichlorophenol contaminated with dioxin. Another NIOSH study found that the 279 trichlorophenol production workers exposed to dioxin did not differ from 258 neighborhood referents with no occupational dioxin exposure on serum glucose overall (51). Workers with the highest half-life extrapolated serum dioxin concentrations, however, had increased adjusted mean serum glucose concentrations compared to referents. An increased risk of diabetes was also seen after adjusting for race, age, body mass index, family history of Type 2 diabetes, and current medications that increase serum glucose concentrations, based on 26 workers and 18 referents who met one of the NIOSH definitions for diabetes. Of the 10 workers with the highest serum dioxin concentrations (>1,500 pg/g lipid), 6 had diabetes mellitus. In contrast, no association was found between glucose intolerance and exposure to dioxins among BASF employees exposed to dioxin (49, 50).

A NIOSH mortality study of 5,172 dioxin-exposed workers at 12 plants showed a statistically significant trend between increased risk of diabetes mortality and decreased cumulative dioxin exposure (55). An international cohort study of 21,863 workers producing or spraying phenoxyacid herbicides and chlorophenols and employed in 36 cohorts from 12 countries found an increased risk of mortality from diabetes among workers with dioxin exposure (57). Mortality from diabetes was increased among residents—and significantly increased among women—who lived in the moderate and low contaminated zones in Seveso, Italy (58, 63).

A 2003 Korean veteran study of 1,224 Vietnam and 154 non-Vietnam veterans in Korea found a statistically significant increased risk of diabetes among Vietnam veterans relative to nonveterans; however, there was no clear trend in prevalence of diabetes across estimated levels of Agent Orange exposure among veterans (62).

Henriksen and colleagues (59) found that the risk of diabetes and glucose abnormalities increased with dioxin among Ranch Hands. The relative risk of diabetes was 1.5 (95% confidence interval: [1.2, 2.0]) among the high-exposed Ranch Hands, an effect that was later shown to be independent of serum triglyceride level (64). In nondiabetic Ranch Hands, insulin abnormalities increased with dioxin levels.

In the AFHS 1992 follow-up examination, Michalek and colleagues (60) studied the influence of dioxin levels on the relation between sex hormone-binding globulin (SHBG) and insulin-related metabolism using lab measures of Ranch Hand cohort and Air Force personnel who were in Southeast Asia (SEA) during the same period but not exposed to herbicides. Among diabetics, no significant correlations were seen between SHBG and either fasting glucose or insulin for any exposure category. Among nondiabetics, SHBG was negatively correlated with insulin for all exposure categories. The authors concluded that a compensatory metabolic relation exists between dioxin and insulin regulation and the negative correlation between SHBG levels and insulin levels suggests that the transported sex hormones are down-regulating insulin release. For nondiabetic veterans in the high exposure category, the geometric mean of insulin level was significantly increased as contrasted with the Comparison group. Fasting serum glucose level was significantly increased among diabetic veterans in the high exposure category; the prevalence of diabetes was similar between the Ranch Hands (12.7%) and the Comparison group (11.2%). Longnecker and Michalek (61) reported an association between serum dioxin levels and diabetes mellitus within a group of Air Force veterans chosen as a comparison cohort for Ranch Hand veterans. Adjusted odds ratios for Type 2 diabetes increased with serum dioxin level; adding serum triglyceride level to the model attenuated the associations.

One hypothesis examined is that dioxin elimination rates explain the relation between diabetes and dioxin concentrations seen in the Ranch Hand study (65). Under this hypothesis, individuals who have a longer dioxin half-life due to slow elimination rates are at an increased risk of diabetes, while individuals who eliminate dioxin more quickly (and have a shorter dioxin half-life) are at a decreased risk of diabetes. Because dioxin is stored in adipose tissue, heavier individuals have a slower elimination rate than lean individuals. The risk of diabetes increased with body fat in Ranch Hand veterans. Michalek and colleagues (65) reported that neither the occurrence of diabetes nor the time of onset to diabetes were related to dioxin elimination after adjustment for dioxin body burden, age, body mass index, family history of diabetes, and smoking history among 343 Ranch Hand veterans.

The epidemiologic studies suggest that any increased risk of Type 2 diabetes from herbicide or dioxin exposure is small when compared to the known predictors—family history, obesity, physical inactivity— for diabetes. Based on its comprehensive review of the literature, one IOM committee found limited or suggestive evidence of an association between exposure to herbicides, including 2,4,5-T and its contaminant dioxin, and Type 2 diabetes (66). This conclusion remained unchanged in the 2002 IOM update (53).

18.1.1.5   *Epidemiology: Reproductive and Developmental Effects*

Serum levels of three endocrine indices—testosterone, LH, and FSH—were examined in relation to current and calculated initial serum dioxin levels in 248 factory workers who experienced significant occupational exposure to dioxin in chemical production plants (67). NIOSH investigators found that current serum dioxin levels were positively and significantly related to both LH and FSH and inversely related to testosterone. In contrast to the NIOSH results, investigators for the AFHS population found no relation between the body burden of dioxin and reproductive or endocrine indices, including serum testosterone, FSH, LH, sperm counts and morphology, and anatomic abnormalities of the testes using categorical measures (68). In the NIOSH cohort, on average, dioxin concentrations were 10 times greater than in the Ranch Hand cohort. When testosterone, FSH, and LH were measured continuously, testosterone decreased with dioxin. After adjusting for military occupation, the investigators found that the relation between dioxin and testosterone was strongest among officers, who were the least exposed, and weakest among enlisted groundcrew, who were the most exposed (69).

Several studies examined sex ratio of children born to parents exposed to dioxin (4, 70-73) and reported conflicting results. An excess of daughters was seen among children born to parents in the Seveso cohort

(70, 72) and in an Austrian chloracne cohort (73). A nonsignificant excess of sons was seen among workers in the NIOSH cohort (71) and in the Ranch Hand cohort (4).

Other studies examined paternal dioxin exposure and reproductive outcomes such as preterm birth, intrauterine growth retardation and infant death (5), spontaneous abortion (71, 74, 75), and stillbirth and birth defects (74, 75). No association was found between dioxin exposure and these reproductive outcomes by any of the investigators.

In 1996, the IOM concluded that limited or suggestive evidence of an association between herbicides used in Vietnam and neural tube defects in the children of veterans (76) exists, a finding that remains unchanged in the 2002 IOM update (53). This conclusion was based in large part on an analysis of birth defects among the offspring of Ranch Hands who reported four neural tube defects among infants, including two cases of spina bifida in infants whose fathers were in the high dioxin exposure group (74). In contrast, no cases of neural tube defects were seen among the Comparison infants. Also in the 2002 update, the IOM concluded that the evidence was inadequate or insufficient to determine whether an association exists between exposure to herbicides used in Vietnam and the following reproductive and developmental outcomes: birth defects other than spina bifida; altered male reproductive hormone concentrations, semen quality, or infertility; spontaneous abortion; stillbirth, neonatal death, or infant death; low birth weight or preterm delivery; altered sex ratio; and childhood cancers (53).

18.1.2   Summary of Previous Analyses of the Air Force Health Study

18.1.2.1   1982 Baseline Examination Summary Results

A laboratory evaluation of the endocrine system was used for analysis in the baseline examination in 1982. Five measures of endocrine status were assessed: T_3 percent uptake, T_4, free thyroxine index (FTI), testosterone, and 2-hour postprandial glucose.

Results showed significant group differences for T_3 percent uptake (abnormally low), predominantly in Ranch Hands 40 years old or younger. The highest percentage of abnormalities was in participants with high body fat. No group difference was noted for elevated 2-hour postprandial glucose values and, as expected, the prevalence of abnormal values was associated with increased age and higher body fat. Lower testosterone values also were associated with increased age and higher body fat. Higher mean testosterone values were significantly more prevalent in the Ranch Hand group. Significant mean shifts were not noted for the T_3 percent uptake, T_4, and the FTI.

18.1.2.2   1985 Follow-up Examination Summary Results

Questionnaire and review-of-systems data for past thyroid disease were similar in both the Ranch Hand and Comparison groups. These historical data were confirmed by a medical records review. Physical examination findings were limited to data from palpation of the thyroid gland and testicles.

Evaluation of the endocrine system was conducted primarily by laboratory testing. The thyroid test battery consisted of T_3 percent uptake and TSH, as determined by radioimmunoassay techniques. Testosterone, initial cortisol, differential cortisol (the difference between the initial and 2-hour cortisol levels), and 2-hour postprandial glucose levels also were analyzed. The T_3 percent uptake data showed no group differences for either mean values or frequency of abnormally low or high values. TSH results revealed a significantly higher mean level in the Ranch Hand group, but this difference was not detected by the discrete analysis of abnormally high TSH results.

Two timed cortisol specimens showed no significant group differences in mean values or the percentage of participants with abnormalities. Differential cortisol showed no significant group differences for non-Blacks or Blacks born before 1942, but Black Ranch Hands born in or after 1942 had a lower mean differential cortisol level than did their Comparisons.

Group means of 2-hour postprandial glucose levels were not statistically different, but analysis of the discrete form of 2-hour postprandial glucose revealed that there was a significantly higher frequency of glucose-impaired Comparisons (at least 140 mg/dL, but less than 200 mg/dL) than Ranch Hands. A variable comprising known diabetics and individuals classified as diabetic by the glucose tolerance test showed no difference between the Ranch Hand and Comparison groups.

18.1.2.3   1987 Follow-up Examination Summary Results

The endocrinology assessment did not disclose any statistically significant differences between the Ranch Hand and Comparison groups. The percentage of participants who indicated problems with current thyroid disease was similar between groups, as were the percentages with thyroid and testicular abnormalities determined by palpation at the physical examination. Ranch Hand and Comparison mean levels were similar for T_3 percent uptake, TSH, FSH, testosterone, and 2-hour postprandial glucose. The percentage of Ranch Hands with abnormal values for these five laboratory variables was higher than the percentage of Comparisons with abnormal values; however, the difference in the percentage of abnormal values between Ranch Hands and Comparisons was not statistically significant for these five laboratory variables. In addition, analyses were performed on a composite diabetes indicator. A participant was considered diabetic for this indicator if he had a verified history of diabetes or had a 2-hour postprandial glucose level of at least 200 mg/dL. The difference in the percentage of Ranch Hands and Comparisons considered diabetic, as determined through this composite diabetes indicator, was not significant.

18.1.2.4   Serum Dioxin Analysis of 1987 Follow-up Examination Summary Results

The endocrinology assessment found a significant positive association between initial dioxin and diabetes prevalence and testes abnormalities. The analyses of dioxin levels in Ranch Hands and Comparisons indicated that the increased risk was apparent for Ranch Hands in the high dioxin category (>33.3 ppt). These Ranch Hands also had significantly higher mean levels of TSH, fasting glucose, and 2-hour postprandial glucose than background Comparisons, as well as lower mean levels of T_3 percent uptake and testosterone. The analyses of these variables in their discrete form found a significant increase in abnormally elevated fasting glucose levels and diabetic 2-hour postprandial glucose levels as both initial dioxin and 1987 dioxin increased. In addition, hemoglobin A1c levels increased as 1987 dioxin levels in Ranch Hands increased.

18.1.2.5   1992 Follow-up Examination Summary Results

The assessment of the endocrine system included an extensive evaluation of thyroid, pancreatic, and gonadal functions and their relation to dioxin. Analyses of thyroid functions did not identify significant differences between Ranch Hands and Comparisons. Similarly, the prevalence of diabetes in the two populations was not significantly different, although significant positive associations were found between time to the onset of diabetes and both lipid-adjusted and whole weight dioxin levels, as measured in 1987.

Significant glucose metabolism results were confined to the dioxin analyses. These results suggested a possible mechanism for dioxin effect on glucose metabolism and the development of diabetes. Diabetic Ranch Hands with high levels of dioxin had significantly higher fasting glucose levels than diabetic Ranch Hands with lower levels of dioxin. Nondiabetic Ranch Hands, on the other hand, exhibited an inverse association between fasting glucose and dioxin and a positive association between 2-hour

postprandial glucose and dioxin. Serum dioxin levels were significantly related to elevated insulin levels in nondiabetic, but not diabetic, Ranch Hands. This was suggestive of a dioxin effect on glucose metabolism with a heightened release of insulin in Ranch Hands with a fully responsive pancreas. When this pancreatic response is no longer effective, elevated glucose levels lead to the clinical diagnosis of diabetes and loss of the dose-response between dioxin and insulin.

Analyses of gonadal functions detected a significant inverse dose-response relation between dioxin and total serum testosterone in Ranch Hands. These results supported those described in the serum dioxin analysis of the 1987 follow-up examination report (77), but the clinical meaning was uncertain.

In conclusion, although the existence of endocrine disorders was comparable in Ranch Hands and Comparisons, the assessment of glucose metabolism showed the possibility of adverse effects from dioxin in relation to glucose intolerance and insulin production.

18.1.2.6   1997 Follow-up Examination Summary Results

The assessment of the endocrine system included an extensive evaluation of thyroid, pancreatic, and gonadal function and their relation to dioxin. A significantly greater percentage of abnormally high TSH values was found in Ranch Hand enlisted groundcrew.

A significant positive association between diabetes and initial and 1987 dioxin was observed. Consistent with previous reports, the prevalence of diabetes for Ranch Hands with high dioxin levels was significantly greater than for Comparisons. A greater percentage of Ranch Hands than Comparisons used insulin to control their Type 2 diabetes, primarily officers and enlisted groundcrew. As initial dioxin levels increased, the percentage of Ranch Hands who required insulin to control their diabetes also increased. A greater percentage of Ranch Hands in the high dioxin category required insulin to control their Type 2 diabetes than did Comparisons. The percentage of participants who treated their diabetes through diet and exercise and the percentage of participants who used oral hypoglycemics increased with 1987 dioxin level.

As initial and 1987 dioxin levels in Ranch Hands increased, both fasting glucose and hemoglobin A1c levels increased, and the time to diabetes onset decreased. The presence of fasting urinary glucose also increased with 1987 dioxin. Increased hemoglobin A1c levels were observed for Ranch Hands in the high dioxin category.

In summary, data from the 1997 AFHS follow-up examination revealed no relation between gonadal disorders and thyroid function and herbicide or dioxin; however, the 1997 follow-up examination results and past results indicated a consistent and potentially meaningful adverse relation between serum dioxin levels and diabetes. A significant dose-response relation was found, where Ranch Hands in the high dioxin category exhibited an increase in diabetes prevalence (relative risk=1.47, 95% confidence interval: [1.00, 2.17]). A dioxin-related increase in severity, a decrease in the time from exposure to first diagnosis, and an increase in fasting glucose and hemoglobin A1c supported this finding. Similar patterns were observed in diabetes and fasting glucose at the 1987 and 1992 follow-up examinations and hemoglobin A1c at the 1992 follow-up examination.

18.1.3   Parameters for the 2002 Endocrinology Assessment

18.1.3.1   Dependent Variables

Questionnaire, physical examination, and laboratory data collected at the AFHS 2002 follow-up examination were used in the endocrinology assessment. The self-reported information collected from the 2002 questionnaire was subsequently verified and analyses were based on the verified data.

18.1.3.1.1 Medical Records Variables

The 2002 questionnaire posed a general screening question on thyroid function and disease. Each participant was asked the following question during the in-person health interview: "Since the date of the last interview, has a doctor told you for the first time that you had thyroid problems?" Medical records review was accomplished to confirm reported problems with thyroid function and to identify any unreported thyroid conditions for each participant that attended the 2002 physical examination. These data from the 2002 physical examination were combined with data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations to form a complete history of thyroid disease for each participant. Thyroid disease was classified according to International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic codes. The ICD-9-CM codes for thyroid disease encompassed 240.0-246.9. Based on the verified data, history of thyroid disease was classified as "yes" or "no." Participants with a pre-SEA history of thyroid disease were excluded from the analysis of thyroid disease history. The analyses performed in this chapter were based on the 1,951 participants who attended the 2002 follow-up examination.

Similar information was asked of each participant regarding diabetes. This information also was verified and combined with previous information. The ICD-9-CM codes for diabetes included 250.00-250.93. Participants verified as diabetics are included in both of the definitions of diabetics below.

Diabetes was defined for the AFHS 2002 follow-up examination using guidelines set forth by the American Diabetes Association (ADA). Under the sponsorship of the ADA, the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (78) recommended that diabetics be defined as participants with a 2-hour postprandial glucose level of 200 mg/dL or greater on two separate occasions, or a fasting glucose level of 126 mg/dL or greater on two separate occasions, or one 2-hour postprandial glucose level of 200 mg/dL or greater and a fasting glucose level of 126 mg/dL or greater on separate occasions. Participants who met this criterion and participants with a verified history of diabetes were combined and designated as diabetic. This definition is termed "2002 AFHS diabetes definition" in subsequent analyses.

Analyses of the composite diabetes indicator, diabetic control, and time to diabetes onset were also carried out using the definition of diabetes used in previous AFHS examinations. Under this definition, participants with a verified history of diabetes were combined with those participants with a 2-hour postprandial glucose level of 200 mg/dL or greater at the 2002 physical examination and classified as "yes" for a composite diabetes indicator variable. Those participants without a verified history of diabetes and with a 2-hour postprandial glucose level of less than 200 mg/dL at the 2002 physical examination were classified as "no." Participants classified as "yes" were designated as diabetics and participants classified as "no" were designated as nondiabetics. This definition is termed "pre-2002 AFHS diabetes definition" in subsequent analyses.

As part of the 2002 questionnaire, questions were asked of diabetics regarding the use of insulin, oral diabetes medication, and diet. This self-reported information was verified and a diabetic severity index was constructed and analyzed for all participants. This index was categorized as "requiring insulin," "oral hypoglycemics," "diet and exercise," or "no treatment" for diabetics and "no diabetes" for nondiabetics.

The analysis of diabetic severity index was carried out twice, using both the pre-2002 AFHS diabetes definition and the 2002 AFHS diabetes definition.

A variable that was termed "time to diabetes onset" was analyzed. This variable combined both diabetics and nondiabetics. For diabetics, time to diabetes onset was the number of years between the date of diagnosis of diabetes and the end date of the last qualifying tour of duty in SEA. For nondiabetics, this variable was the number of years between the date of the 2002 follow-up physical examination and the end date of the last qualifying tour of duty in SEA. The "time to diabetes onset" variable was defined in this way to allow statistical analysis using the proportional hazards model, as described in Chapter 7. The analysis of time to diabetes onset was carried out twice, using both the pre-2002 AFHS diabetes definition and the 2002 AFHS diabetes definition.

Participants with a pre-SEA history of diabetes were excluded from the composite diabetes indicator, diabetic control, and time to diabetes onset analyses. Type 1 diabetics would also have been excluded, but all of the diabetics in the AFHS were verified as Type 2 diabetics.

18.1.3.1.2 Physical Examination Variable

The physical examination of endocrine function included manual palpation of the thyroid gland and testes. Thyroid abnormalities consisted of enlarged gland, tenderness, presence of nodules, or a thyroidectomy (ICD-9-CM procedure codes X06.2-X06.6). Testicular abnormalities consisted of atrophied or absent testes because of a post-SEA orchiectomy (orchiectomies were coded as ICD-9-CM procedure codes X62.3-X62.42). Participants with a pre-SEA history of thyroid disease and participants who were currently taking thyroid medication (ICD-9-CM medication codes 68:36.04 and 68:36.08) were excluded from the analysis of the thyroid gland. For the analysis of testicular abnormalities, participants with a pre-SEA orchiectomy or participants with a missing testicle because of an undescended testicle, a congenital absence, or as a result of injury (ICD diagnostic codes 752.51-752.8) were excluded.

18.1.3.1.3 Laboratory Variables

For the AFHS 2002 follow-up examination, 17 laboratory variables were analyzed statistically in the endocrinology assessment for all participants. In addition, diabetics were tested for the presence or absence of islet cell antibodies, but no participant had islet cell antibodies present and further statistical analysis was not conducted.

TSH (μIU/mL), T_4 (ng/dL), total testosterone (ng/dL), LH (mIU/mL), and FSH (mIU/mL) were measured using Bayer Centaur® equipment. Abbott AXSYM® equipment was used to measure estradiol (pg/mL). Anti-thyroid antibodies were analyzed using passive hemagglutination assay. Free testosterone (pg/mL) was conducted by radioimmunoassay.

Measurements for fasting and 2-hour postprandial glucose (mg/dL) were taken using Dade RxL® equipment. Analyses for 2-hour postprandial urinary glucose were conducted by dipstick methods using Bayer Atlas® equipment. DPC Immulite® equipment was used to measure serum insulin (fasting and 2-hour postprandial). The 100-gram glucose load for the postprandial assays was standardized by the use of Glucola® and was not given to participants with a verified history of diabetes unless requested by the participant.

Participants classified as "diabetic" under the 2002 AFHS diabetes definition, as described above, and participants who stated that they were diabetic at the time of the 2002 physical examination were tested for hemoglobin A1c (percent), C-peptide (ng/mL), proinsulin (pmol/L), and glutamic acid decarboxylase antibodies (GADA). Bio-Rad Variant® equipment was used to measure hemoglobin A1c (percent), and

C-peptide was measured by DPC Immulite® equipment. Presence or absence of GADA was determined by radioimmunoassay. Presence or absence of islet cell antibodies was determined by immunofluorescence antibodies. Proinsulin was determined by Associates Regional and University Pathology Lab in Salt Lake City using enzyme immunoassay methods.

All laboratory variables were analyzed in both discrete and continuous forms except for anti-thyroid antibodies, 2-hour postprandial urinary glucose, and GADA. These variables were analyzed as discrete variables only and were categorized as "present" or "absent."

TSH and insulin (fasting and 2-hour postprandial) were categorized as "abnormally low," "normal," and "abnormally high," based on Scripps laboratory cutpoints. The analysis of 2-hour postprandial glucose, which was performed for nondiabetics only, was coded as "normal" and "impaired." Those participants without a verified history of diabetes, using the 2002 AFHS diabetes definition, and with a 2-hour postprandial glucose level of at least 140 mg/dL or a fasting glucose level of at least 110 mg/dL at the 2002 physical examination were classified as "impaired." Those participants without a verified history of diabetes, a 2-hour postprandial glucose level less than 140 mg/dL, and a fasting glucose level of less than 110 mg/dL at the 2002 physical examination were classified as "normal."

All other laboratory results were dichotomized as "normal" or "abnormal" (abnormally high for all variables, except for free T_4, total testosterone, and free testosterone, which were classified according to abnormally low values). A sparse number of abnormally high values for free T_4, total testosterone, and free testosterone existed.

Participants with a pre-SEA history of thyroid disease, a thyroidectomy, or who took thyroid medication were excluded from the analyses of TSH, free T_4, and anti-thyroid antibodies. For total and free testosterone, estradiol, LH, and FSH, participants with bilateral orchiectomies (pre-SEA or post-SEA) and participants currently taking testosterone medication (ICD-9-CM medication code 68:08) were excluded.

Participants with pre-SEA diabetes were excluded from the analysis of fasting glucose and fasting insulin. Participants who had a verified history of diabetes or participants who stated that they had diabetes at the time of the 2002 physical examination were not tested for 2-hour postprandial glucose, 2-hour postprandial urinary glucose, and 2-hour postprandial insulin, and consequently these participants were excluded from the statistical analyses of these variables. In addition, participants classified as "diabetic" under the ADA criteria described above were excluded from the analyses of 2-hour postprandial glucose, 2-hour postprandial urinary glucose, and 2-hour postprandial insulin. Nondiabetics were excluded from the analysis of hemoglobin A1c, C-peptide, proinsulin, and GADA.

18.1.3.2   Covariates

The endocrinology assessment included the effects of age, race, military occupation, and body mass index (kg/m^2) in the adjusted analyses of all variables. Lifetime cigarette smoking history (pack-years), the ratio of the waist measurement to the hip measurement at the 2002 physical examination, and a covariate characterizing family history of diabetes also were included for the diabetes-related variables. The dependent variables included the composite diabetes indicator, diabetic control, time to diabetes onset, fasting and 2-hour postprandial glucose, 2-hour postprandial urinary glucose, fasting and 2-hour postprandial insulin, hemoglobin A1c, C-peptide, proinsulin, and GADA.

Age, race, and military occupation were determined from military records. Body mass index was calculated as weight/(height)^2, where the weight was measured in kilograms and the height was measured in meters at the physical examination (79). For purposes of covariate associations for discrete dependent variables, body mass index was dichotomized as "not obese" ($\leq$30 kg/m^2) and "obese" (>30 kg/m^2).

Lifetime cigarette smoking history was based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 2002 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

A measurement of each participant's hips and waist (in cm) was taken at the 2002 physical examination. This information was used to construct a waist-to-hip ratio that was used as a covariate for diabetes-related dependent variables.

Each participant was asked in the 2002 questionnaire whether anyone in his immediate family ever had diabetes or sugar diabetes. A family history of diabetes covariate was constructed from the responses to this question and used in adjusted analyses of all diabetic-related dependent variables.

18.1.4 Statistical Methods

Table 18-1 summarizes the statistical analysis performed for the 2002 endocrinology assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, exclusions, and statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 18-1.

The analysis of time to diabetes onset was based on a proportional hazards model, in which time to onset was modeled as a linear combination of exposure variables and covariates. Instead of mean values, the summary statistic provided was the 10th percentile of the hazard function. Because approximately 20 percent of the participants at the 2002 follow-up examination were diabetic, the 10th percentile is being used to represent an estimate of the approximate median time to diabetes onset. This observed time represents an estimate of the number of years that have elapsed since the end of the last qualifying tour until 10 percent of participants in the cohort of interest were diagnosed as diabetic. Further details on the statistical procedures used for the analysis of time to onset are discussed in Chapter 7, Statistical Methods.

A large number of estradiol measurements below the machine sensitivity limit of 10 pg/mL were present. The measurements above the sensitivity limit exhibited a positively skewed distribution, so a logarithmic transformation was applied to the measurements above the sensitivity limit to achieve an approximate normal distribution. The logarithmic transformation, however, could not be applied to the nonquantified measurements below the sensitivity limit. Consequently, the continuous form of only the estradiol measurements above the sensitivity limit was analyzed. The discrete form of estradiol was analyzed using Scripps laboratory cutpoints, as shown in Table 18-1.

Table 18-1. Statistical Analysis for the Endocrinology Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Past Thyroid Disease	MR-V	D	Yes No	(1)	(a)	U:LR A:LR
Composite Diabetes Indicator (2002 AFHS diabetes definition)	MR-V/ LAB	D	• Diabetic: past history of diabetes, as diagnosed previously by a physician, or ≥200 mg/dL 2-hour postprandial glucose on two separate occasions, or ≥126 mg/dL fasting glucose on two separate occasions, or one 2-hour postprandial glucose ≥200 mg/dL and one fasting glucose ≥126 mg/dL on two separate occasions • Nondiabetic: Otherwise	(2)	(b)	U:LR,CS A:LR
Composite Diabetes Indicator (pre-2002 AFHS diabetes definition)	MR-V/ LAB	D	• Diabetic: past history of diabetes or ≥200 mg/dL 2-hour postprandial glucose • Nondiabetic: Otherwise	(2)	(b)	U:LR,CS A:LR
Diabetic Control (2002 AFHS diabetes definition)	MR-V/ LAB	D	Requiring Insulin Oral Hypoglycemics Diet and Exercise No Treatment Nondiabetic	(2)	(b)	U:PR,CS A:PR
Diabetic Control (pre-2002 AFHS diabetes definition)	MR-V/ LAB	D	Requiring Insulin Oral Hypoglycemics Diet and Exercise No Treatment Nondiabetic	(2)	(b)	U:PR,CS A:PR
Time to Diabetes Onset (years) (2002 AFHS diabetes definition)	MR-V/ LAB/ MIL	C	--	(2)	(b)	U:PH A:PH
Time to Diabetes Onset (years) (2002 AFHS pre-diabetes definition)	MR-V/ LAB/ MIL	C	--	(2)	(b)	U:PH A:PH

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Thyroid Gland	PE	D	Abnormal Normal	(1)	(c)	U:LR,CS A:LR
Testicular Examination	PE	D	Abnormal Normal	(1)	(d)	U:LR,CS A:LR
TSH (µIU/mL)	LAB	C/D	Abnormal Low: <0.35 Normal: 0.35-5.5 Abnormal High: >5.5	(1)	(e)	U:PR,CS,GLM,TT A:PR,GLM
Free T$_4$ (ng/dL)	LAB	C/D	Low: <0.89 Normal: ≥0.89	(1)	(e)	U:LR,CS,GLM,TT A:LR,GLM
Anti-Thyroid Antibodies	LAB	D	Present Absent	(1)	(e)	U:LR,CS A:LR
Fasting Glucose (mg/dL)	LAB	C/D	High: >110 Normal: ≤110	(2)	(b)	U:LR,CS,GLM,TT A:LR,GLM
2-hour Postprandial Glucose (mg/dL)	LAB	C/D	Impaired: ≥140 Normal: <140	(2)	(f)	U:LR,CS,GLM,TT A:LR,GLM
2-hour Postprandial Urinary Glucose	LAB	D	Present Absent	(2)	(f)	U:LR,CS A:LR
Fasting Insulin (µIU/mL)	LAB	C/D	Abnormal Low: <6 Normal: 6-27 Abnormal High: >27	(2)	(b)	U:PR,GLM A:PR,GLM
2-hour Postprandial Insulin (µIU/mL)	LAB	C/D	Abnormal Low: <18 Normal: 18-56 Abnormal High: >56	(2)	(f)	U:PR,GLM A:PR,GLM
Hemoglobin A1c (percent)	LAB	C/D	High: >6.0 Normal: ≤6.0	(2)	(g)	U:LR,CS,GLM,TT A:LR,GLM
C-peptide (ng/mL)	LAB	C/D	High: >5 Normal: ≤5	(2)	(g)	U:LR,CS,GLM,TT A:LR,GLM
Proinsulin (pmol/L)	LAB	C/D	High: >26.8 Normal: ≤26.8	(2)	(g)	U:LR,CS,GLM,TT A:LR,GLM
GADA	LAB	D	Present Absent	(2)	(g)	U:LR,CS A:LR
Total Testosterone (ng/dL)	LAB	C/D	Low: <241 Normal: ≥241	(1)	(h)	U:LR,CS,GLM,TT A:LR,GLM
Free Testosterone (pg/mL)	LAB	C/D	Low: <6 Normal: ≥6	(1)	(h)	U:LR,CS,GLM,TT A:LR,GLM
Estradiol (pg/mL)	LAB	C/D	High: >52 Normal: ≤52	(1)	(h)	U:LR,CS,GLM,TT A:LR,GLM

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
LH (mIU/mL)	LAB	C/D	High: >12 Normal: ≤12	(1)	(h)	U:LR,CS,GLM,TT A:LR,GLM
FSH (mIU/mL)	LAB	C/D	High: >18.1 Normal: ≤18.1	(1)	(h)	U:LR,CS,GLM,TT A:LR,GLM

[a]Covariates:
(1) age, race, military occupation, body mass index.
(2) age, race, military occupation, body mass index, lifetime cigarette smoking history, waist-to-hip ratio, family history of diabetes.

[b]Exclusions:
(a) participants with a pre-SEA history of thyroid disease.
(b) participants with a pre-SEA history of diabetes.
(c) participants with a pre-SEA history of thyroid disease, participants currently taking thyroid medication.
(d) participants with a pre-SEA orchiectomy (full or partial), participants with a testicle absent (undescended or congenital absence).
(e) participants with a pre-SEA history of thyroid disease, participants with a thyroidectomy, participants currently taking thyroid medication.
(f) participants classified as diabetic under the 2002 AFHS diabetes definition.
(g) all nondiabetics using the 2002 AFHS diabetes definition.
(h) participants with a bilateral orchiectomy (pre-SEA or post-SEA), participants currently taking testosterone medication.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	C/D	Born ≥ 1942 Born < 1942
Race	MIL	D	Black Non-Black
Military Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Body Mass Index (kg/m^2)	PE	C/D	Not Obese: ≤30 Obese: >30
Lifetime Cigarette Smoking History (pack-years)	Q-SR	C/D	0 >0–10 >10
Waist-to-hip Ratio	PE	C/D	>1 ≤1
Family History of Diabetes	Q-SR	D	Yes No

Abbreviations

Data Source: LAB: 2002 laboratory results
                                         MIL: Air Force military records
                                         MR-V: Medical records (verified)
                                         PE: 2002 physical examination
                                         Q-SR: 2002 health questionnaire (self-reported)

Data Form: C: Continuous form of dependent variable
                                         D: Discrete form of dependent variable or covariate
                                         C/D: Continuous and discrete forms of dependent variable; appropriate form for analysis
                                              (either continuous or discrete) of covariate

Statistical Analysis: U: Unadjusted analysis
                                         A: Adjusted analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
                                         GLM: General linear models analysis
                                         LR: Logistic regression analysis
                                         PH: Proportional hazards analysis
                                         PR: Polytomous logistic regression analysis
                                         TT: Two-sample t-test

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Four models were examined for each dependent variable given in Table 18-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for covariates. These covariates are given in Table 18-1. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. In an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-4, the median level of exposure to dioxin was highest for enlisted groundcrew, followed by enlisted flyers, then officers.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the CDC using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in parts per trillion (ppt) on a lipid weight basis (80). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2. A statistical adjustment for body mass

index at the time of the participant's blood measurement of dioxin was included in this model to account for body mass index-related differences in elimination rate (81).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. Another category was examined by combining the low and high Ranch Hand categories. This combination is referred to in the tables as the "low plus high Ranch Hand" category. These five categories—Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the four Ranch Hand categories and the dependent variable in the Comparison category was examined. As in Model 2, a statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables. One Ranch Hand without a dioxin measure was excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The term "unadjusted" was used in the text and tables as follows: Models 1 and 4 did not adjust for any covariates. Models 2 and 3 adjusted only for body mass index at the time of the blood measurement for dioxin. The term "adjusted" was used in the text and tables as follows: Models 1 and 4 adjusted for the covariates shown in Table 18-1 unless otherwise specified by a footnote to the table. Models 2 and 3 additionally adjusted only for body mass index at the time of the blood measurement for dioxin.

Table 18-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants that were excluded from analyses is given.

Table 18-2. Number of Participants Excluded or with Missing Data for the Endocrinology Assessment

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Thyroid Gland	DEP	1	2	4	1	1	2
Testicular Abnormality	DEP	10	14	6	10	10	14
2-hour Postprandial Measurements[d]	DEP	126	190	88	126	126	190
Hemoglobin A1c[e]	DEP	609	903	312	608	608	903
Diabetic Assay Panel – other components[e]	DEP	608	903	311	607	607	903
Body Mass Index	COV	1	0	0	1	1	0
Lifetime Cigarette Smoking History	COV	0	3	0	0	0	3
Waist-to-hip Ratio	COV	1	1	0	1	1	1

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Family History of Diabetes	COV	8	9	6	8	8	9
Pre-SEA History of Thyroid Disease	EXC	7	7	4	7	7	7
Pre-SEA Diabetes	EXC	1	1	1	1	1	1
Currently Taking Thyroid Medication	EXC	39	74	18	39	39	74
Thyroidectomy	EXC	10	17	3	10	10	17
Bilateral Orchiectomy	EXC	1	0	1	1	1	0
Unilateral Testicle Absent (undescended, congenital, or from injury)	EXC	2	1	1	2	2	1
Testosterone Medication	EXC	6	13	3	6	6	13

[a]777 Ranch Hands and 1,174 Comparisons for group.

[b]424 Ranch Hands for initial dioxin; 776 Ranch Hands for 1987 dioxin.

[c]776 Ranch Hands and 1,174 Comparisons for categorized dioxin.

[d]Included 2-hour postprandial glucose, 2-hour postprandial urinary glucose, and 2-hour postprandial insulin. Most participants who were excluded were diabetics.

[e]Other components of diabetic assay panel (in addition to hemoglobin A1c) included C-peptide, proinsulin, and GADA. Most participants who were excluded were nondiabetics.

Note: DEP = Dependent variable.
          COV = Covariate.
          EXC = Exclusion.

18.2 RESULTS

18.2.1 Dependent Variable-covariate Associations

The endocrine dependent variables were tested for associations with each of the covariates used in the adjusted analyses. The complete results are presented in Appendix F, Table F-10. These associations were pairwise between the dependent variable and the covariate and were not adjusted for any other covariates. A brief summary of the pattern of significant ($p \leq 0.05$) dependent variable-covariate associations is described in the following paragraphs.

Older participants had a higher prevalence of diabetes, which necessitated an increase in all forms of treatment for their diabetes. The time to the onset of diabetes also was shorter for older participants. Age was significantly associated with the results of the testicular examination, TSH in its continuous form, and hemoglobin A1c in its continuous form. Older participants had a higher percentage of abnormal testicular examination results. TSH levels increased with age and hemoglobin A1c levels decreased with age. Fasting glucose, 2-hour postprandial glucose, LH, and FSH in both continuous and discrete forms increased with age. Fasting insulin, proinsulin, total testosterone, and free testosterone in their discrete and continuous forms each decreased with age.

A higher percentage of Black participants were classified as diabetic. Race also was significantly associated with diabetic control. Black participants controlled their diabetes with oral hypoglycemics twice as often as non-Black participants. Time to the onset of diabetes also was shorter for Black participants.

Race was associated with the continuous form of TSH, fasting glucose, 2-hour postprandial insulin, hemoglobin A1c, C-peptide, and estradiol. The mean fasting glucose, 2-hour postprandial insulin, hemoglobin A1c, and estradiol values were higher for Blacks than non-Blacks. Non-Black participants had a higher mean TSH and C-peptide value than Black participants. The discrete forms of 2-hour postprandial insulin and C-peptide were also significantly associated with race. Black participants were more likely to have abnormally high 2-hour postprandial insulin values than non-Black participants. Non-Black participants were more than three times as likely to have abnormally high C-peptide values as Black participants.

Officers had higher mean TSH and FSH values than enlisted flyers or enlisted groundcrew. Officers had lower mean fasting glucose, fasting insulin, 2-hour postprandial insulin, hemoglobin A1c, and free testosterone levels than enlisted flyers or enlisted groundcrew. Enlisted flyers had a higher mean 2-hour postprandial glucose value than officers or enlisted groundcrew.

More officers had abnormally low fasting insulin and 2-hour postprandial insulin than enlisted participants. In addition, officers had a greater percentage of high FSH values than enlisted participants. Fewer officers than enlisted flyers and enlisted groundcrew had abnormal results for 2-hour postprandial glucose, 2-hour postprandial urinary glucose, and hemoglobin A1c. Fewer officers were classified as diabetic based on the pre-2002 AFHS diabetes definition than enlisted participants. Enlisted flyers had a smaller percentage of abnormally low free testosterone levels than officers or enlisted groundcrew.

Obese participants had a higher prevalence of diabetes, which required more treatment, and a shorter time to onset more often than participants who were not obese. Body mass index was inversely associated with free T_4, total testosterone, and free testosterone in their continuous and discrete forms. Body mass index was also positively associated with fasting glucose, 2-hour postprandial glucose, fasting insulin, 2-hour postprandial insulin, C-peptide, and proinsulin in their continuous and discrete forms.

The heaviest lifetime cigarette smokers (in terms of pack-years) had the highest prevalence of diabetes and required an increase in all forms of treatment for their diabetes. The time to the onset of diabetes also was shorter for the heaviest lifetime cigarette smokers. Participants who were heavier smokers throughout their lives had the highest prevalence of abnormally high measurements for fasting glucose, 2-hour postprandial insulin, and C-peptide. Fasting glucose, fasting insulin, and C-peptide increased with lifetime cigarette smoking.

The waist-to-hip ratio was positively associated with all diabetic-related variables except hemoglobin A1c and GADA. Participants with larger waist-to-hip ratios had the higher prevalence of diabetes, which required more treatment, and developed diabetes sooner than participants with smaller waist-to-hip ratios. In addition, more participants with waist-to-hip ratios greater than one had abnormally high fasting insulin and 2-hour postprandial insulin levels than participants with waist-to-hip ratios less than or equal to one.

Participants who had a family history of diabetes had a higher prevalence of diabetes than participants who did not have a family history of diabetes. This higher prevalence of diabetes was associated with an increase in all forms of treatment for their diabetes. The time to the onset of diabetes also was shorter for participants who had a family history of diabetes.

Participants with a family history of diabetes had higher mean fasting glucose, 2-hour postprandial glucose, fasting insulin, and 2-hour postprandial insulin values than participants with no family history of diabetes. Higher percentages of abnormally high fasting glucose, fasting insulin, and 2-hour postprandial insulin values were seen among participants with a family history of diabetes than among participants with no family history of diabetes.

18.2.2   Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 18-1. Dependent variables are grouped into three sections: (1) the medical records variables, derived from the questionnaire that was administered in the 2002 follow-up and previous AFHS examinations and verified by a review of medical records, (2) variables obtained during the 2002 physical examination, and (3) laboratory variables.

18.2.2.1   Medical Records Variables

18.2.2.1.1 Past Thyroid Disease

All unadjusted and adjusted analyses of past thyroid disease for Models 1 through 4 were nonsignificant (Table 18-3(a-h): $p>0.06$ for all analyses).

Table 18-3. Analysis of Past Thyroid Disease

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*83 (10.8)*	*0.81 (0.61,1.07)*	*0.136*
	Comparison	*1,167*	*152 (13.0)*		
Officer	Ranch Hand	304	36 (11.8)	0.89 (0.57,1.39)	0.616
	Comparison	459	60 (13.1)		
Enlisted Flyer	Ranch Hand	132	14 (10.6)	0.80 (0.39,1.60)	0.523
	Comparison	185	24 (13.0)		
Enlisted Groundcrew	Ranch Hand	334	33 (9.9)	0.73 (0.47,1.14)	0.168
	Comparison	523	68 (13.0)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,936*	*0.80 (0.61,1.07)*	*0.133*
Officer	762	0.89 (0.57,1.39)	0.607
Enlisted Flyer	317	0.79 (0.39,1.59)	0.505
Enlisted Groundcrew	857	0.74 (0.47,1.14)	0.173

Table 18-3. Analysis of Past Thyroid Disease (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a,b]**	**p-Value**
Low	140	15 (10.7)	1.05 (0.82,1.33)	0.715
Medium	141	11 (7.8)		
High	139	15 (10.8)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	**Adjusted Relative Risk** **(95% C.I.)[a]**	**p-Value**
420	1.16 (0.87,1.53)	0.321

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	**n**	**Number (%)** **Yes**	**Unadjusted Relative Risk** **(95% C.I.)[a,b]**	**p-Value**
Comparison	1,167	152 (13.0)		
Background RH	349	42 (12.0)	0.94 (0.65,1.36)	0.754
Low RH	209	21 (10.0)	0.74 (0.46,1.20)	0.220
High RH	211	20 (9.5)	0.68 (0.41,1.11)	0.124
Low plus High RH	420	41 (9.8)	0.71 (0.49,1.02)	0.065

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-3. Analysis of Past Thyroid Disease (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,167		
Background RH	348	0.94 (0.65,1.37)	0.748
Low RH	209	0.73 (0.45,1.18)	0.198
High RH	211	0.69 (0.41,1.14)	0.147
Low plus High RH	420	0.71 (0.49,1.02)	0.066

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	31 (12.0)	0.97 (0.84,1.12)	0.709
Medium	256	27 (10.5)		
High	254	25 (9.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	0.98 (0.83,1.16)	0.828

[a]Relative risk for a twofold increase in 1987 dioxin.

18.2.2.1.2 Composite Diabetes Indicator (2002 AFHS Diabetes Definition)

The unadjusted and adjusted Model 1, 2, and 3 analyses of the composite diabetes indicator using the 2002 AFHS diabetes definition did not show any significant results (Table 18-4(a-f): p>0.06 for each analysis). A significant association between 1987 dioxin and the composite diabetes indicator was seen in both the unadjusted and adjusted Model 4 analyses (Table 18-4(g,h): Unadjusted Relative Risk [RR]=1.27, p<0.001; Adjusted RR=1.29, p=0.001). The percentage of diabetic participants in the low, medium, and high 1987 dioxin categories were 9.6, 20.2, and 24.9, respectively.

Table 18-4. Analysis of Composite Diabetes Indicator (2002 AFHS Diabetes Definition)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Diabetic	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*776*	*141 (18.2)*	*0.93 (0.74,1.17)*	*0.544*
	Comparison	*1,173*	*226 (19.3)*		
Officer	Ranch Hand	306	50 (16.3)	0.95 (0.64,1.40)	0.783
	Comparison	462	79 (17.1)		
Enlisted Flyer	Ranch Hand	133	29 (21.8)	0.92 (0.54,1.57)	0.762
	Comparison	185	43 (23.2)		
Enlisted Groundcrew	Ranch Hand	337	62 (18.4)	0.91 (0.65,1.30)	0.617
	Comparison	526	104 (19.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,929*	*0.93 (0.72,1.19)*	*0.567*
Officer	763	0.89 (0.59,1.35)	0.590
Enlisted Flyer	311	0.93 (0.52,1.66)	0.799
Enlisted Groundcrew	855	0.96 (0.66,1.40)	0.840

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Diabetic	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	30 (21.4)	1.06 (0.88,1.27)	0.520
Medium	142	34 (23.9)		
High	141	35 (24.8)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	1.25 (0.99,1.58)	0.061

[a]Relative risk for a twofold increase in initial dioxin.

Table 18-4. *Analysis of Composite Diabetes Indicator (2002 AFHS Diabetes Definition) (Continued)*

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Diabetic	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,173	226 (19.3)		
Background RH	352	42 (11.9)	0.71 (0.49,1.03)	0.073
Low RH	210	47 (22.4)	1.14 (0.78,1.68)	0.496
High RH	213	52 (24.4)	1.13 (0.78,1.63)	0.531
Low plus High RH	423	99 (23.4)	1.13 (0.85,1.51)	0.392

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,162		
Background RH	349	0.74 (0.50,1.10)	0.134
Low RH	206	1.13 (0.75,1.69)	0.567
High RH	211	1.25 (0.83,1.88)	0.294
Low plus High RH	417	1.18 (0.87,1.61)	0.282

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Diabetic	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	25 (9.6)	1.27 (1.13,1.42)	<0.001**
Medium	258	52 (20.2)		
High	257	64 (24.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value$\leq$0.010).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
766	1.29 (1.10,1.51)	0.001**

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

18.2.2.1.3 Composite Diabetes Indicator (Pre-2002 AFHS Diabetes Definition)

No group differences were seen in the unadjusted and adjusted Model 1 analysis of the composite diabetes indicator using the pre-2002 AFHS diabetes definition (Table 18-5(a,b): p>0.26 for each analysis).

The unadjusted Model 2 analysis revealed no significant association between the composite diabetes indicator and initial dioxin (Table 18-5(c): p=0.286). After adjusting for covariates the results became significant (Table 18-5(d): Adjusted RR=1.34, p=0.010). The percentages of diabetic participants in the low, medium, and high initial dioxin categories were 22.1, 27.5, and 27.0, respectively. Both the unadjusted and adjusted Model 3 analyses of the composite diabetes indicator revealed no significant contrasts (Table 18-5(e,f): p>0.12 for each analysis).

A significant association between 1987 dioxin and the composite diabetes indicator was seen in both the unadjusted and adjusted Model 4 analyses (Table 18-5(g,h): Unadjusted RR=1.24, p<0.001; Adjusted RR=1.27, p=0.001). The percentages of diabetic participants in the low, medium, and high 1987 dioxin categories were 12.3, 22.1, and 27.6, respectively.

Table 18-5. Analysis of Composite Diabetes Indicator (Pre-2002 AFHS Diabetes Definition)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Diabetic	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*776*	*160 (20.6)*	*0.92 (0.73,1.14)*	*0.441*
	Comparison	*1,173*	*259 (22.1)*		
Officer	Ranch Hand	306	61 (19.9)	1.10 (0.77,1.59)	0.595
	Comparison	462	85 (18.4)		
Enlisted Flyer	Ranch Hand	133	31 (23.3)	0.80 (0.48,1.34)	0.392
	Comparison	185	51 (27.6)		
Enlisted Groundcrew	Ranch Hand	337	68 (20.2)	0.83 (0.59,1.16)	0.269
	Comparison	526	123 (23.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,929*	*0.91 (0.72,1.16)*	*0.442*
Officer	763	1.07 (0.72,1.58)	0.753
Enlisted Flyer	311	0.78 (0.45,1.37)	0.387
Enlisted Groundcrew	855	0.85 (0.59,1.22)	0.381

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Diabetic	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	31 (22.1)	1.10 (0.92,1.31)	0.286
Medium	142	39 (27.5)		
High	141	38 (27.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	1.34 (1.07,1.68)	0.010**

[a]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Diabetic	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,173	259 (22.1)		
Background RH	352	52 (14.8)	0.76 (0.54,1.08)	0.123
Low RH	210	50 (23.8)	1.04 (0.71,1.50)	0.855
High RH	213	58 (27.2)	1.10 (0.77,1.58)	0.584
Low plus High RH	423	108 (25.5)	1.07 (0.81,1.41)	0.635

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,162		
Background RH	349	0.81 (0.56,1.16)	0.247
Low RH	206	0.97 (0.66,1.44)	0.897
High RH	211	1.19 (0.80,1.75)	0.390
Low plus High RH	417	1.08 (0.80,1.45)	0.625

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Diabetic	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	32 (12.3)	1.24 (1.11,1.38)	<0.001**
Medium	258	57 (22.1)		
High	257	71 (27.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)**[a]	**p-Value**
766	1.27 (1.09,1.47)	0.001**

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value$\leq$0.010).

18.2.2.1.4 *Diabetic Control (2002 AFHS Diabetes Definition)*

The unadjusted and adjusted Model 1 analyses of diabetic control, using the 2002 AFHS diabetes definition, were nonsignificant (Table 18-6(a,b): p>0.16 for each analysis).

Significant positive relations were seen between initial dioxin and Ranch Hands requiring insulin in both the unadjusted and adjusted Model 2 analyses (Table 18-6(c,d): Unadjusted RR=1.76, p=0.004; Adjusted RR=2.78, p<0.001). The percentages of Ranch Hands requiring insulin in the low, medium, and high initial dioxin categories were 0.7, 2.1, and 7.1, respectively. The remaining contrasts in the unadjusted and adjusted Model 2 analyses were nonsignificant (Table 18-6(c,d): p>0.07 for each contrast).

Among participants requiring insulin to control diabetes, a significant difference between the percentage of Ranch Hands in the high dioxin category and Comparisons was seen in both the unadjusted and adjusted Model 3 analyses (Table 18-6(e,f): Unadjusted RR=2.11, p=0.037; Adjusted RR=2.66, p=0.016). Ranch Hands in the high dioxin category had a higher percentage of participants requiring insulin than did the Comparisons (5.6 % and 2.5 %, respectively). All other contrasts in both the unadjusted and adjusted Model 3 analyses were nonsignificant (Table 18-6(e,f): p$\geq$0.07 for each analysis).

The unadjusted and adjusted Model 4 analyses each revealed a significant positive association between 1987 dioxin and the percentage of diabetics who used oral hypoglycemics to treat diabetes (Table 18-6(g,h): Unadjusted RR=1.32, p<0.001; Adjusted RR=1.32, p=0.006). A positive association between 1987 dioxin and the percentage of diabetics requiring insulin also was observed in both the unadjusted and adjusted Model 4 analyses (Table 18-6(g,h): Unadjusted RR=1.43, p=0.007; Adjusted RR=1.53, p=0.021). The percentages of Ranch Hands taking oral hypoglycemics in the low, medium, and high 1987 dioxin categories were 3.9, 11.2, and 14.0, respectively. Among Ranch Hands requiring insulin to control diabetes, the percentages in the low, medium, and high 1987 dioxin categories were 1.9, 1.2, and 5.1, respectively. The remaining two contrasts in each of the unadjusted and adjusted Model 4 analyses were nonsignificant (Table 18-6(g,h): p>0.15 for each contrast).

Table 18-6. Analysis of Diabetic Control (2002 AFHS Diabetes Definition)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED										
			Number (%)						Unadjusted	
Occupational Category	Group	n	Nondiabetic	No Treatment	Diet and Exercise	Oral Hypo-glycemics	Requiring Insulin	Contrast vs. Nondiabetic	Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*776*	*635 (81.8)*	*24 (3.1)*	*21 (2.7)*	*75 (9.7)*	*21 (2.7)*	*No Treatment*	*0.89 (0.53,1.50)*	*0.673*
	Comparison	*1,173*	*947 (80.7)*	*40 (3.4)*	*35 (3.0)*	*122 (10.4)*	*29 (2.5)*	*Diet and Exercise*	*0.89 (0.52,1.55)*	*0.692*
								Oral Hypoglycemics	*0.92 (0.68,1.24)*	*0.576*
								Requiring Insulin	*1.08 (0.61,1.91)*	*0.792*
Officer	Ranch Hand	306	256 (83.7)	10 (3.3)	7 (2.3)	25 (8.2)	8 (2.6)	No Treatment	1.25 (0.53,2.93)	0.613
	Comparison	462	383 (82.9)	12 (2.6)	14 (3.0)	42 (9.1)	11 (2.4)	Diet and Exercise	0.75 (0.30,1.88)	0.537
								Oral Hypoglycemics	0.89 (0.53,1.50)	0.662
								Requiring Insulin	1.09 (0.43,2.74)	0.858
Enlisted Flyer	Ranch Hand	133	104 (78.2)	6 (4.5)	7 (5.3)	13 (9.8)	3 (2.3)	No Treatment	1.37 (0.43,4.35)	0.599
	Comparison	185	142 (76.8)	6 (3.2)	6 (3.2)	25 (13.5)	6 (3.2)	Diet and Exercise	1.59 (0.52,4.88)	0.415
								Oral Hypoglycemics	0.71 (0.35,1.45)	0.349
								Requiring Insulin	0.68 (0.17,2.79)	0.595
Enlisted Groundcrew	Ranch Hand	337	275 (81.6)	8 (2.4)	7 (2.1)	37 (11.0)	10 (3.0)	No Treatment	0.56 (0.24,1.27)	0.165
	Comparison	526	422 (80.2)	22 (4.2)	15 (2.9)	55 (10.5)	12 (2.3)	Diet and Exercise	0.72 (0.29,1.78)	0.472
								Oral Hypoglycemics	1.03 (0.66,1.61)	0.888
								Requiring Insulin	1.28 (0.55,3.00)	0.572

Table 18-6. Analysis of Diabetic Control (2002 AFHS Diabetes Definition) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED

Occupational Category	n	Contrast	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,929*	*No Treatment vs. Nondiabetic*	*0.87 (0.51,1.46)*	*0.591*
		Diet and Exercise vs. Nondiabetic	*0.86 (0.49 ,1.51)*	*0.596*
		Oral Hypoglycemics vs. Nondiabetic	*0.93 (0.67,1.29)*	*0.665*
		Requiring Insulin vs. Nondiabetic	*1.09 (0.60,1.97)*	*0.775*
Officer	763	No Treatment vs. Nondiabetic	1.15 (0.48,2.73)	0.751
		Diet and Exercise vs. Nondiabetic	0.70 (0.28,1.77)	0.449
		Oral Hypoglycemics vs. Nondiabetic	0.84 (0.48,1.46)	0.535
		Requiring Insulin vs. Nondiabetic	1.03 (0.40,2.62)	0.952
Enlisted Flyer	311	No Treatment vs. Nondiabetic	1.34 (0.41,4.35)	0.630
		Diet and Exercise vs. Nondiabetic	1.83 (0.56,5.99)	0.317
		Oral Hypoglycemics vs. Nondiabetic	0.68 (0.31,1.47)	0.325
		Requiring Insulin vs. Nondiabetic	0.58 (0.11,3.08)	0.520
Enlisted Groundcrew	855	No Treatment vs. Nondiabetic	0.56 (0.24,1.29)	0.174
		Diet and Exercise vs. Nondiabetic	0.65 (0.25,1.71)	0.381
		Oral Hypoglycemics vs. Nondiabetic	1.14 (0.71,1.83)	0.595
		Requiring Insulin vs. Nondiabetic	1.40 (0.58,3.37)	0.458

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

| Initial Dioxin Category | | Initial Dioxin Category Summary Statistics | | | | | Analysis Results for Log_2 (Initial Dioxin) | | |
| | | | Number (%) | | | | | | |
Initial Dioxin Category	n	Nondiabetic	No Treatment	Diet and Exercise	Oral Hypoglycemics	Requiring Insulin	Contrast vs. Nondiabetic	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	110 (78.6)	12 (8.6)	2 (1.4)	15 (10.7)	1 (0.7)	No Treatment	0.69 (0.46,1.03)	0.072
Medium	142	108 (76.1)	4 (2.8)	7 (4.9)	20 (14.1)	3 (2.1)	Diet and Exercise	0.89 (0.56,1.42)	0.636
High	141	106 (75.2)	4 (2.8)	3 (2.1)	18 (12.8)	10 (7.1)	Oral Hypoglycemics	1.09 (0.86,1.37)	0.476
							Requiring Insulin	1.76 (1.20,2.58)	0.004**

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

| | | Analysis Results for Log_2 (Initial Dioxin) | |
n	Contrast	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	No Treatment vs. Nondiabetic	0.77 (0.48,1.23)	0.279
	Diet and Exercise vs. Nondiabetic	0.88 (0.48,1.62)	0.688
	Oral Hypoglycemics vs. Nondiabetic	1.21 (0.91,1.62)	0.195
	Requiring Insulin vs. Nondiabetic	2.78 (1.61,4.82)	<0.001**

[a]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Results were not adjusted for race because of the sparse number of Black Ranch Hands requiring treatment for diabetes.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Number (%)				
		Nondiabetic	No Treatment	Diet and Exercise	Oral Hypoglycemics	Requiring Insulin
Comparison	1,173	947 (80.7)	40 (3.4)	35 (3.0)	122 (10.4)	29 (2.5)
Background RH	352	310 (88.1)	4 (1.1)	9 (2.6)	22 (6.3)	7 (2.0)
Low RH	210	163 (77.6)	13 (6.2)	7 (3.3)	25 (11.9)	2 (1.0)
High RH	213	161 (75.6)	7 (3.3)	5 (2.4)	28 (13.2)	12 (5.6)
Low plus High RH	423	324 (76.6)	20 (4.7)	12 (2.8)	53 (12.5)	14 (3.3)

Dioxin Category	No Treatment vs. Nondiabetic		Diet and Exercise vs. Nondiabetic		Oral Hypoglycemics vs. Nondiabetic		Requiring Insulin vs. Nondiabetic	
	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison								
Background RH	0.38 (0.13,1.08)	0.070	0.89 (0.42,1.87)	0.751	0.72 (0.44,1.17)	0.185	0.89 (0.38,2.06)	0.776
Low RH	1.80 (0.93,3.50)	0.081	1.15 (0.50,2.63)	0.745	1.11 (0.67,1.81)	0.693	0.39 (0.09,1.66)	0.201
High RH	0.86 (0.37,1.98)	0.725	0.77 (0.29,1.99)	0.583	1.08 (0.67,1.74)	0.746	2.11 (1.04,4.26)	0.037*
Low plus High RH	1.24 (0.70,2.22)	0.462	0.94 (0.48,1.84)	0.848	1.09 (0.75,1.59)	0.638	0.91 (0.39,2.12)	0.830

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-6. Analysis of Diabetic Control (2002 AFHS Diabetes Definition) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	No Treatment vs. Nondiabetic		Diet and Exercise vs. Nondiabetic		Oral Hypoglycemics vs. Nondiabetic		Requiring Insulin vs. Nondiabetic	
		Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,162								
Background RH	349	0.38 (0.13,1.09)	0.071	0.88 (0.41,1.91)	0.746	0.78 (0.46,1.31)	0.344	0.89 (0.37,2.12)	0.791
Low RH	206	1.74 (0.88,3.44)	0.110	0.97 (0.39,2.38)	0.944	1.16 (0.69,1.95)	0.585	0.37 (0.09,1.61)	0.185
High RH	211	0.90 (0.38,2.12)	0.803	0.86 (0.32,2.31)	0.761	1.19 (0.70,2.03)	0.517	2.66 (1.20,5.87)	0.016*
Low plus High RH	417	1.24 (0.69,2.25)	0.469	0.91 (0.45,1.85)	0.796	1.17 (0.79,1.75)	0.428	1.00 (0.42,2.39)	0.992

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-6. Analysis of Diabetic Control (2002 AFHS Diabetes Definition) (Continued)

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

1987 Dioxin Category	1987 Dioxin Category Summary Statistics Number (%)						Analysis Results for Log_2 (1987 Dioxin)		
	n	Nondiabetic	No Treatment	Diet and Exercise	Oral Hypoglycemics	Requiring Insulin	Contrast vs. Nondiabetic	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	235 (90.4)	4 (1.5)	6 (2.3)	10 (3.9)	5 (1.9)	No Treatment	1.20 (0.94,1.54)	0.151
Medium	258	206 (79.8)	13 (5.0)	7 (2.7)	29 (11.2)	3 (1.2)	Diet and Exercise	1.03 (0.78,1.35)	0.851
High	257	193 (75.1)	7 (2.7)	8 (3.1)	36 (14.0)	13 (5.1)	Oral Hypoglycemics	1.32 (1.14,1.53)	<0.001**
							Requiring Insulin	1.43 (1.10,1.85)	0.007**

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED

n	Analysis Results for Log_2 (1987 Dioxin)		
	Contrast	Adjusted Relative Risk (95% C.I.)[a]	p-Value
766	No Treatment vs. Nondiabetic	1.17 (0.83,1.64)	0.365
	Diet and Exercise vs. Nondiabetic	1.00 (0.71,1.42)	0.987
	Oral Hypoglycemics vs. Nondiabetic	1.32 (1.08,1.60)	0.006**
	Requiring Insulin vs. Nondiabetic	1.53 (1.07,2.19)	0.021*

[a]Relative risk for a twofold increase in 1987 dioxin.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: Results were not adjusted for race because of the sparse number of Black Ranch Hands requiring treatment for diabetes.

18.2.2.1.5 Diabetic Control (Pre-2002 AFHS Diabetes Definition)

The unadjusted and adjusted Model 1 analyses of diabetic control, using the pre-2002 AFHS diabetes definition, revealed no overall group differences between Ranch Hands and Comparisons (Table 18-7(a,b): $p > 0.36$ for each contrast). After stratifying by occupation, however, each of the unadjusted and adjusted Model 1 analyses revealed a significant difference between the percentage of Ranch Hand and Comparison enlisted groundcrew who used no treatment for diabetes (Table 18-7(a,b): Unadjusted RR=0.51, p=0.036; Adjusted RR=0.51, p=0.037). Among Ranch Hand enlisted groundcrew, 4.2 percent used no treatment for diabetes versus 7.8 percent of Comparisons. The remaining contrasts were nonsignificant (Table 18-7(a,b): $p > 0.10$ for each unadjusted and adjusted contrast).

The unadjusted and adjusted Model 2 analyses each revealed a significant positive relation between initial dioxin and Ranch Hands who require insulin to control diabetes (Table 18-7(c,d): Unadjusted RR=1.79, p=0.003; Adjusted RR=2.90, p<0.001). The percentages of Ranch Hands requiring insulin in the low, medium, and high initial dioxin categories were 0.7, 2.1, and 7.1, respectively. All other unadjusted and adjusted Model 2 results were nonsignificant (Table 18-7(c,d): $p > 0.10$ for each contrast).

Among participants requiring insulin to control diabetes, a significant difference between the percentage of Ranch Hands in the high dioxin category and Comparisons was seen in both the unadjusted and adjusted Model 3 analyses (Table 18-7(e,f): Unadjusted RR=2.11, p=0.038; Adjusted RR=2.64, p=0.017). Ranch Hands in the high dioxin category had a higher percentage of participants requiring insulin than did the Comparisons (5.6% and 2.5%, respectively). All other contrasts in both the unadjusted and adjusted Model 3 analyses were nonsignificant (Table 18-7(e,f): $p > 0.16$ for each analysis).

The unadjusted and adjusted Model 4 analyses each revealed a significant positive association between 1987 dioxin and Ranch Hands taking oral hypoglycemics (Table 18-7(g,h): Unadjusted RR=1.32, p<0.001; Adjusted RR=1.32, p=0.005), as well as a significant positive association between 1987 dioxin and Ranch Hands requiring insulin to control diabetes (Table 18-7(g,h): Unadjusted RR=1.43, p=0.007; Adjusted RR=1.54, p=0.019). The percentages of Ranch Hands taking oral hypoglycemics in the low, medium, and high 1987 dioxin categories were 3.9, 11.2, and 14.0, respectively. The percentages of Ranch Hands requiring insulin in the low, medium, and high 1987 dioxin categories were 1.9, 1.2, and 5.1, respectively. The remaining contrasts in the unadjusted and adjusted Model 4 analyses were nonsignificant (Table 18-7(g,h): $p > 0.17$ for each contrast).

Table 18-7. Analysis of Diabetic Control (Pre-2002 AFHS Diabetes Definition)

			Number (%)					Contrast vs. Nondiabetic	Unadjusted Relative Risk (95% C.I.)	p-Value
Occupational Category	Group	n	Nondiabetic	No Treatment	Diet and Exercise	Oral Hypo-glycemics	Requiring Insulin			
All	*Ranch Hand*	*776*	*616 (79.4)*	*42 (5.4)*	*22 (2.8)*	*75 (9.7)*	*21 (2.7)*	*No Treatment*	*0.85 (0.58,1.26)*	*0.430*
	Comparison	*1,173*	*914 (77.9)*	*73 (6.2)*	*35 (3.0)*	*122 (10.4)*	*29 (2.5)*	*Diet and Exercise*	*0.93 (0.54,1.61)*	*0.801*
								Oral Hypoglycemics	*0.91 (0.67,1.24)*	*0.555*
								Requiring Insulin	*1.07 (0.61,1.90)*	*0.805*
Officer	Ranch Hand	306	245 (80.1)	20 (6.5)	8 (2.6)	25 (8.2)	8 (2.6)	No Treatment	1.71 (0.89,3.30)	0.109
	Comparison	462	377 (81.6)	18 (3.9)	14 (3.0)	42 (9.1)	11 (2.4)	Diet and Exercise	0.88 (0.36,2.13)	0.775
								Oral Hypoglycemics	0.92 (0.54,1.54)	0.741
								Requiring Insulin	1.12 (0.44,2.82)	0.811
Enlisted Flyer	Ranch Hand	133	102 (76.7)	8 (6.0)	7 (5.3)	13 (9.8)	3 (2.3)	No Treatment	0.75 (0.30,1.86)	0.535
	Comparison	185	134 (72.4)	14 (7.6)	6 (3.2)	25 (13.5)	6 (3.2)	Diet and Exercise	1.53 (0.50,4.70)	0.455
								Oral Hypoglycemics	0.68 (0.33,1.40)	0.298
								Requiring Insulin	0.66 (0.16,2.69)	0.559
Enlisted Groundcrew	Ranch Hand	337	269 (79.8)	14 (4.2)	7 (2.1)	37 (11.0)	10 (3.0)	No Treatment	0.51 (0.27,0.96)	0.036*
	Comparison	526	403 (76.6)	41 (7.8)	15 (2.9)	55 (10.5)	12 (2.3)	Diet and Exercise	0.70 (0.28,1.74)	0.441
								Oral Hypoglycemics	1.01 (0.65,1.57)	0.973
								Requiring Insulin	1.25 (0.53,2.93)	0.610

*: Statistically significant (0.010<p-value≤0.050).

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Table 18-7. Analysis of Diabetic Control (Pre-2002 AFHS Diabetes Definition) (Continued)

Occupational Category	n	Contrast	Adjusted Relative Risk (95% C.I.)	p-Value
(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED				
All	*1,929*	*No Treatment vs. Nondiabetic*	*0.83 (0.56,1.24)*	*0.361*
		Diet and Exercise vs. Nondiabetic	*0.89 (0.51,1.56)*	*0.690*
		Oral Hypoglycemics vs. Nondiabetic	*0.92 (0.67,1.28)*	*0.626*
		Requiring Insulin vs. Nondiabetic	*1.08 (0.60,1.96)*	*0.797*
Officer	763	No Treatment vs. Nondiabetic	1.63 (0.84,3.19)	0.149
		Diet and Exercise vs. Nondiabetic	0.82 (0.34,2.01)	0.672
		Oral Hypoglycemics vs. Nondiabetic	0.88 (0.51,1.53)	0.645
		Requiring Insulin vs. Nondiabetic	1.07 (0.42,2.73)	0.886
Enlisted Flyer	311	No Treatment vs. Nondiabetic	0.71 (0.28,1.80)	0.477
		Diet and Exercise vs. Nondiabetic	1.74 (0.53,5.71)	0.360
		Oral Hypoglycemics vs. Nondiabetic	0.64 (0.30,1.39)	0.260
		Requiring Insulin vs. Nondiabetic	0.55 (0.10,2.92)	0.480
Enlisted Groundcrew	855	No Treatment vs. Nondiabetic	0.51 (0.27,0.96)	0.037*
		Diet and Exercise vs. Nondiabetic	0.63 (0.24,1.66)	0.350
		Oral Hypoglycemics vs. Nondiabetic	1.09 (0.68,1.76)	0.713
		Requiring Insulin vs. Nondiabetic	1.35 (0.56,3.26)	0.507

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

| Initial Dioxin Category | n | Initial Dioxin Category Summary Statistics — Number (%) | | | | | Analysis Results for Log$_2$ (Initial Dioxin) | | |
		Nondiabetic	No Treatment	Diet and Exercise	Oral Hypoglycemics	Requiring Insulin	Contrast vs. Nondiabetic	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	109 (77.9)	13 (9.3)	2 (1.4)	15 (10.7)	1 (0.7)	No Treatment	0.89 (0.65,1.21)	0.462
Medium	142	103 (72.5)	9 (6.3)	7 (4.9)	20 (14.1)	3 (2.1)	Diet and Exercise	0.91 (0.57,1.44)	0.680
High	141	103 (73.1)	7 (5.0)	3 (2.1)	18 (12.8)	10 (7.1)	Oral Hypoglycemics	1.12 (0.89,1.40)	0.352
							Requiring Insulin	1.79 (1.22,2.62)	0.003**

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

| | | Analysis Results for Log$_2$ (Initial Dioxin) | |
n	Contrast	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	No Treatment vs. Nondiabetic	1.09 (0.75,1.58)	0.644
	Diet and Exercise vs. Nondiabetic	0.91 (0.50,1.67)	0.768
	Oral Hypoglycemics vs. Nondiabetic	1.27 (0.95,1.70)	0.104
	Requiring Insulin vs. Nondiabetic	2.90 (1.68,5.01)	<0.001**

[a]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Results were not adjusted for race because of the sparse number of Black Ranch Hands requiring treatment for diabetes.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Number (%)				
		Nondiabetic	No Treatment	Diet and Exercise	Oral Hypoglycemics	Requiring Insulin
Comparison	1,173	914 (77.9)	73 (6.2)	35 (3.0)	122 (10.4)	29 (2.5)
Background RH	352	300 (85.2)	13 (3.7)	10 (2.8)	22 (6.3)	7 (2.0)
Low RH	210	160 (76.2)	16 (7.6)	7 (3.3)	25 (11.9)	2 (1.0)
High RH	213	155 (72.8)	13 (6.1)	5 (2.4)	28 (13.2)	12 (5.6)
Low plus High RH	423	315 (74.5)	29 (6.9)	12 (2.8)	53 (12.5)	14 (3.3)

Dioxin Category	No Treatment vs. Nondiabetic		Diet and Exercise vs. Nondiabetic		Oral Hypoglycemics vs. Nondiabetic		Requiring Insulin vs. Nondiabetic	
	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison								
Background RH	0.65 (0.35,1.20)	0.172	0.99 (0.48,2.04)	0.984	0.72 (0.44,1.18)	0.194	0.89 (0.38,2.07)	0.785
Low RH	1.20 (0.68,2.14)	0.527	1.12 (0.49,2.57)	0.791	1.06 (0.65,1.75)	0.808	0.38 (0.09,1.61)	0.188
High RH	0.91 (0.49,1.70)	0.769	0.76 (0.29,1.98)	0.577	1.08 (0.67,1.74)	0.747	2.11 (1.04,4.26)	0.038*
Low plus High RH	1.05 (0.66,1.66)	0.846	0.92 (0.47,1.82)	0.814	1.07 (0.74,1.56)	0.712	0.90 (0.39,2.09)	0.803

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-7. Analysis of Diabetic Control (Pre-2002 AFHS Diabetes Definition) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY — ADJUSTED										
		No Treatment vs. Nondiabetic		Diet and Exercise vs. Nondiabetic		Oral Hypoglycemics vs. Nondiabetic		Requiring Insulin vs. Nondiabetic		
Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,162								
Background RH	349	0.69 (0.37,1.29)	0.241	0.98 (0.47,2.08)	0.966	0.79 (0.47,1.33)	0.378	0.90 (0.38,2.15)	0.813
Low RH	206	1.06 (0.59,1.92)	0.838	0.93 (0.38,2.29)	0.876	1.10 (0.65,1.85)	0.728	0.35 (0.08,1.54)	0.165
High RH	211	0.89 (0.47,1.69)	0.723	0.86 (0.32,2.32)	0.760	1.18 (0.69,2.02)	0.540	2.64 (1.19,5.83)	0.017*
Low plus High RH	417	0.97 (0.61,1.55)	0.905	0.89 (0.44,1.82)	0.754	1.14 (0.76,1.70)	0.522	0.98 (0.41,2.33)	0.959

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.010 < p\text{-value} \le 0.050$).

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\le$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\le$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

1987 Dioxin Category		1987 Dioxin Category Summary Statistics Number (%)					Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin Category	n	Nondiabetic	No Treatment	Diet and Exercise	Oral Hypoglycemics	Requiring Insulin	Contrast vs. Nondiabetic	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	228 (87.7)	10 (3.9)	7 (2.7)	10 (3.9)	5 (1.9)	No Treatment	1.14 (0.94,1.39)	0.174
Medium	258	201 (77.9)	18 (7.0)	7 (2.7)	29 (11.2)	3 (1.2)	Diet and Exercise	1.00 (0.76,1.31)	0.982
High	257	186 (72.4)	14 (5.5)	8 (3.1)	36 (14.0)	13 (5.1)	Oral Hypoglycemics	1.32 (1.14,1.53)	<0.001**
							Requiring Insulin	1.43 (1.10,1.85)	0.007**

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED

n	Analysis Results for Log$_2$ (1987 Dioxin)		
n	Contrast	Adjusted Relative Risk (95% C.I.)[a]	p-Value
766	No Treatment vs. Nondiabetic	1.17 (0.90,1.52)	0.238
	Diet and Exercise vs. Nondiabetic	0.97 (0.69,1.37)	0.867
	Oral Hypoglycemics vs. Nondiabetic	1.32 (1.09,1.61)	0.005**
	Requiring Insulin vs. Nondiabetic	1.54 (1.07,2.21)	0.019*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: Results were not adjusted for race because of the sparse number of Black Ranch Hands requiring treatment for diabetes.

18.2.2.1.6 Time to Diabetes Onset (2002 AFHS Diabetes Definition)

The time to diabetes onset from time of duty in SEA, using the 2002 AFHS diabetes definition, did not differ significantly between Ranch Hands and Comparisons in the Model 1 unadjusted and adjusted analyses (Table 18-8(a,b): p>0.26 for all analyses).

The Model 2 unadjusted and adjusted analyses did not reveal a significant relation between initial dioxin and time to diabetes onset (Table 18-8(c,d): p>0.05 for all analyses).

The Model 3 unadjusted and adjusted analyses revealed a significant difference in time to diabetes onset between Ranch Hands in the background dioxin category and Comparisons (Table 18-8(e,f): Unadjusted Hazard Ratio=0.67, p=0.017; Adjusted Hazard Ratio=0.69, p=0.030, respectively). The time to diabetes onset was significantly longer for Ranch Hands in the background dioxin category than for Comparisons. The 10th percentile for time to diabetes onset was 33.17 years for Ranch Hands in the background category and 28.41 years for Comparisons.

The unadjusted and adjusted Model 4 analyses revealed a significant association between time to diabetes onset and 1987 dioxin (Table 18-8(g,h): Unadjusted Hazard Ratio=1.25, p<0.001; Adjusted Hazard Ratio=1.28, p<0.001, respectively). In each analysis, the time to diabetes onset was shorter for Ranch Hands with higher 1987 dioxin levels. The 10th percentile of Ranch Hands in the low 1987 dioxin category was 34.42 years compared to 26.75 years for Ranch Hands in the medium dioxin category and 23.67 years for Ranch Hands in the high dioxin category.

Table 18-8. Analysis of Time to Diabetes Onset (years) (2002 AFHS Diabetes Definition)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	10th Percentile	Unadjusted Hazard Ratio (95% C.I.)	p-Value
All	*Ranch Hand*	*776*	*27.67*	*0.89 (0.72,1.10)*	*0.265*
	Comparison	*1,173*	*28.41*		
Officer	Ranch Hand	306	28.08	0.91 (0.64,1.30)	0.613
	Comparison	462	28.16		
Enlisted Flyer	Ranch Hand	133	27.09	0.85 (0.53,1.36)	0.496
	Comparison	185	27.08		
Enlisted Groundcrew	Ranch Hand	337	27.83	0.89 (0.65,1.22)	0.459
	Comparison	526	28.92		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Hazard Ratio (95% C.I.)	p-Value
All	*1,929*	*0.92 (0.75,1.15)*	*0.468*
Officer	763	0.90 (0.63,1.29)	0.580
Enlisted Flyer	311	0.89 (0.54,1.45)	0.630
Enlisted Groundcrew	855	0.96 (0.70,1.32)	0.800

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	**n**	**10th Percentile**	**Unadjusted Hazard Ratio (95% C.I.)[a,b]**	**p-Value**
Low	140	25.75	1.04 (0.90,1.20)	0.628
Medium	142	25.91		
High	141	21.58		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Hazard ratio for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	**Adjusted Hazard Ratio (95% C.I.)[a]**	**p-Value**
417	1.20 (1.00,1.45)	0.055

[a]Hazard ratio for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	10th Percentile	Unadjusted Hazard Ratio (95% C.I.)[a,b]	p-Value
Comparison	1,173	28.41		
Background RH	352	33.17	0.67 (0.48,0.93)	0.017*
Low RH	210	25.75	1.14 (0.84,1.57)	0.401
High RH	213	23.67	1.07 (0.79,1.45)	0.661
Low plus High RH	423	25.08	1.10 (0.87,1.40)	0.413

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Hazard ratio and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Hazard Ratio (95% C.I.)[a]	p-Value
Comparison	1,162		
Background RH	349	0.69 (0.49,0.96)	0.030*
Low RH	206	1.12 (0.81,1.55)	0.494
High RH	211	1.09 (0.78,1.50)	0.622
Low plus High RH	417	1.10 (0.86,1.41)	0.437

[a]Hazard ratio and confidence interval relative to Comparisons.

*: Statistically significant ($0.010 < \text{p-value} \le 0.050$).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\le$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\le$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	10th Percentile	Adjusted Hazard Ratio (95% C.I.)[a]	p-Value
Low	260	34.42	1.25 (1.13,1.38)	<0.001**
Medium	258	26.75		
High	257	23.67		

[a]Hazard ratio for a twofold increase in 1987 dioxin.

**: Statistically significant ($\text{p-value} \le 0.010$).

Note: Low = $\le$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Hazard Ratio (95% C.I.)[a]	p-Value
766	1.28 (1.12,1.46)	<0.001**

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant ($\text{p-value} \le 0.010$).

18.2.2.1.7 Time to Diabetes Onset (Pre-2002 AFHS Diabetes Definition)

The analyses based on the pre-2002 AFHS diabetes definition yielded very similar results to those attained when using the 2002 AFHS diabetes definition. No significant findings were revealed in both the unadjusted and adjusted analyses of Model 1 (Table 18-9(a,b): p>0.12 for all analyses).

Similarly, the unadjusted analysis of Model 2 did not reveal significant findings in the time to diabetes onset (Table 18-9(c): p=0.54). When adjusted for covariates, a significant relation between initial dioxin and time to diabetes onset was revealed (Table 18-9(d): Adjusted Hazard Ratio=1.21, p=0.033). The time to diabetes onset was significantly shorter for Ranch Hands with higher initial dioxin levels. Ten percent of Ranch Hands in the low initial dioxin category had developed diabetes by 25.75 years after the last qualifying tour of duty compared to 25.91 years for Ranch Hands in the medium dioxin category and 21.58 years for Ranch Hands in the high dioxin category.

Both unadjusted and adjusted analyses of Model 3 revealed significant differences in time to diabetes onset between Ranch Hands in the background dioxin category and Comparisons (Table 18-9(e,f): Unadjusted Hazard Ratio=0.69, p=0.016; Adjusted Hazard Ratio=0.71, p=0.030, respectively). Thus, the time to diabetes onset was significantly longer for Ranch Hands in the background dioxin category (10th percentile of time to diabetes onset: 33.08 years) than for Comparisons (10th percentile of time to diabetes onset: 28.41 years). No other comparisons were significant (Table 18-9(e,f): p>0.59 for all analyses).

The unadjusted and adjusted Model 4 analyses each revealed significant associations between time to diabetes onset and 1987 dioxin (Table 18-9(g,h): Unadjusted Hazard Ratio=1.23, p<0.001; Adjusted Hazard Ratio=1.26, p<0.001, respectively). In both analyses, the time to diabetes onset was shorter for Ranch Hands with higher 1987 dioxin levels. The 10th percentile of Ranch Hands in the low 1987 dioxin category was 33.50 years compared to 26.75 years for Ranch Hands in the medium dioxin category and 23.67 years for Ranch Hands in the high dioxin category.

Table 18-9. Analysis of Time to Diabetes Onset (years) (Pre-2002 AFHS Diabetes Definition)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	10th Percentile (years)	Unadjusted Hazard Ratio (95% C.I.)	p-Value
All	*Ranch Hand*	*776*	*27.67*	*0.86 (0.70,1.04)*	*0.126*
	Comparison	*1,173*	*28.41*		
Officer	Ranch Hand	306	28.08	1.00 (0.72,1.40)	0.987
	Comparison	462	28.16		
Enlisted Flyer	Ranch Hand	133	27.09	0.73 (0.47,1.15)	0.173
	Comparison	185	27.08		
Enlisted Groundcrew	Ranch Hand	337	27.83	0.82 (0.61,1.10)	0.180
	Comparison	526	28.92		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Hazard Ratio (95% C.I.)	p-Value
All	*1,929*	*0.89 (0.73,1.09)*	*0.246*
Officer	763	0.99 (0.71,1.39)	0.969
Enlisted Flyer	311	0.75 (0.47,1.21)	0.240
Enlisted Groundcrew	855	0.87 (0.65,1.18)	0.379

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	10th Percentile (years)	Unadjusted Hazard Ratio (95% C.I.)[a,b]	p-Value
Low	140	25.75	1.05 (0.91,1.20)	0.542
Medium	142	25.91		
High	141	21.58		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Hazard ratio for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Hazard Ratio (95% C.I.)[a]	p-Value
417	1.21 (1.02,1.45)	0.033*

[a]Hazard ratio for a twofold increase in initial dioxin.

*: Statistically significant ($0.010 < $ p-value ≤ 0.050).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	10th Percentile (years)	Unadjusted Hazard Ratio (95% C.I.)[a,b]	p-Value
Comparison	1,173	28.41		
Background RH	352	33.08	0.69 (0.51,0.93)	0.016*
Low RH	210	25.75	1.09 (0.80,1.47)	0.593
High RH	213	23.67	1.03 (0.77,1.37)	0.858
Low plus High RH	423	25.08	1.05 (0.84,1.32)	0.651

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Hazard ratio and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Hazard Ratio (95% C.I.)[a]	p-Value
Comparison	1,162		
Background RH	349	0.71 (0.52,0.97)	0.030*
Low RH	206	1.04 (0.76,1.43)	0.798
High RH	211	1.02 (0.75,1.39)	0.890
Low plus High RH	417	1.03 (0.82,1.30)	0.795

[a]Hazard ratio and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**10th Percentile (years)**	**Adjusted Hazard Ratio (95% C.I.)[a]**	**p-Value**
Low	260	33.50	1.23 (1.12,1.35)	<0.001**
Medium	258	26.75		
High	257	23.67		

[a]Hazard ratio for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Hazard Ratio (95% C.I.)[a]**	**p-Value**
766	1.26 (1.12,1.43)	<0.001**

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

18.2.2.2   Physical Examination Variables

18.2.2.2.1 Thyroid Gland

The unadjusted and adjusted Model 1 and Model 2 analyses of thyroid gland showed no significant results (Table 18-10(a-d): p>0.06 for each analysis).

The unadjusted Model 3 analysis of the thyroid gland revealed a significant difference between Comparisons and Ranch Hands in the low and high categories combined (Table 18-10(e): p=0.044). Two Ranch Hands (0.5%) in the low and high dioxin categories combined and 24 (2.2%) Comparisons had an abnormal thyroid gland. After adjusting for covariates, no significant results were seen (Table 18-10(f): p>0.30 for each contrast).

The Model 4 unadjusted and adjusted analyses revealed no significant relation between 1987 dioxin and thyroid gland abnormalities (Table 18-10(g,h): p>0.16 for each analysis).

Table 18-10. Analysis of Thyroid Gland

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*734*	*8 (1.1)*	*0.49 (0.22,1.10)*	*0.069*
	Comparison	*1,093*	*24 (2.2)*		
Officer	Ranch Hand	285	3 (1.1)	0.55 (0.14,2.09)	0.381
	Comparison	422	8 (1.9)		
Enlisted Flyer	Ranch Hand	126	0 (0.0)	--	0.372[a]
	Comparison	174	3 (1.7)		
Enlisted Groundcrew	Ranch Hand	323	5 (1.5)	0.59 (0.21,1.66)	0.313
	Comparison	497	13 (2.6)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal thyroid gland.

--: Results were not presented because of the sparse number of participants with an abnormal thyroid gland.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,827*	*0.50 (0.22,1.11)*	*0.073*
Officer	707	0.55 (0.14,2.08)	0.375
Enlisted Flyer	300	--	--
Enlisted Groundcrew	820	0.59 (0.21,1.68)	0.324

--: Results were not presented because of the sparse number of participants with an abnormal thyroid gland.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	134	2 (1.5)	0.30 (0.04,2.25)	0.134
Medium	139	0 (0.0)		
High	131	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 18-10. Analysis of Thyroid Gland (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
404	0.27 (0.04,1.84)	0.094

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with an abnormal thyroid gland.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,093	24 (2.2)		
Background RH	329	6 (1.8)	0.81 (0.33,2.01)	0.649
Low RH	201	2 (1.0)	0.45 (0.11,1.92)	0.281
High RH	203	0 (0.0)	--	0.065[c]
Low plus High RH	404	2 (0.5)	--	0.044*[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormal thyroid gland.

--: Results were not presented because of the sparse number of participants with an abnormal thyroid gland.

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-10. Analysis of Thyroid Gland (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,093		
Background RH	329	0.90 (0.36,2.27)	0.822
Low RH	201	0.47 (0.11,2.01)	0.306
High RH	203	--	--
Low plus High RH	404	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with an abnormal thyroid gland.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	244	3 (1.2)	0.76 (0.49,1.19)	0.229
Medium	245	5 (2.0)		
High	244	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
733	0.73 (0.47,1.13)	0.162

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with an abnormal thyroid gland.

18.2.2.2.2 Testicular Examination

All unadjusted and adjusted analyses of the testicular examination in Models 1 through 4 were nonsignificant (Table 18-11(a-h): p>0.07 for each analysis).

Table 18-11. Analysis of Testicular Examination

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*764*	*56 (7.3)*	*1.10 (0.77,1.56)*	*0.618*
	Comparison	*1,158*	*78 (6.7)*		
Officer	Ranch Hand	300	21 (7.0)	0.93 (0.53,1.64)	0.807
	Comparison	455	34 (7.5)		
Enlisted Flyer	Ranch Hand	131	14 (10.7)	1.55 (0.70,3.41)	0.280
	Comparison	181	13 (7.2)		
Enlisted Groundcrew	Ranch Hand	333	21 (6.3)	1.07 (0.60,1.89)	0.826
	Comparison	522	31 (5.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,922*	*1.09 (0.76,1.56)*	*0.647*
Officer	755	0.92 (0.52,1.63)	0.780
Enlisted Flyer	312	1.47 (0.66,3.27)	0.345
Enlisted Groundcrew	855	1.11 (0.62,1.98)	0.736

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	137	7 (5.1)	1.12 (0.86,1.45)	0.413
Medium	139	13 (9.4)		
High	140	12 (8.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
416	1.34 (0.97,1.85)	0.073

[a]Relative risk for a twofold increase in initial dioxin.

Table 18-11. Analysis of Testicular Examination (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,158	78 (6.7)		
Background RH	347	24 (6.9)	1.04 (0.65,1.68)	0.862
Low RH	206	14 (6.8)	1.01 (0.56,1.81)	0.985
High RH	210	18 (8.6)	1.28 (0.75,2.20)	0.361
Low plus High RH	416	32 (7.7)	1.14 (0.74,1.75)	0.557

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,158		
Background RH	347	1.00 (0.61,1.63)	0.989
Low RH	206	0.89 (0.49,1.61)	0.690
High RH	210	1.53 (0.86,2.70)	0.145
Low plus High RH	416	1.17 (0.75,1.82)	0.499

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	16 (6.3)	1.08 (0.91,1.27)	0.375
Medium	252	17 (6.7)		
High	255	23 (9.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 18-11. Analysis of Testicular Examination (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (1987 Dioxin) | |
| | Adjusted Relative Risk | |
n	**(95% C.I.)**[a]	**p-Value**
763	1.11 (0.90,1.36)	0.344

[a]Relative risk for a twofold increase in 1987 dioxin.

18.2.2.3 Laboratory Variables

18.2.2.3.1 TSH (Continuous)

Both the unadjusted and adjusted Model 1 analyses of TSH in its continuous form showed significant overall group differences (Table 18-12(a,b): difference of means=0.108 µIU/mL, p=0.023; difference of adjusted means=0.096 µIU/mL, p=0.024). The overall adjusted mean TSH values were 1.653 µIU/mL for Ranch Hands and 1.557 µIU/mL for Comparisons. After stratifying by military occupation, unadjusted and adjusted analyses revealed group differences within the officer stratum (Table 18-12(a,b): difference of means=0.211 µIU/mL, p=0.010; difference of adjusted means=0.189 µIU/mL, p=0.009). Among officers, Ranch Hands had a higher adjusted mean TSH value than Comparisons (1.778 µIU/mL and 1.589 µIU/mL, respectively).

The unadjusted and adjusted Model 2 analyses revealed no significant relation between TSH and initial dioxin (Table 18-12(c,d): p>0.54 for each analysis).

Model 3 unadjusted and adjusted analyses each revealed a significant difference in mean TSH levels between Ranch Hands in the background dioxin category and Comparisons (Table 18-12(e,f): difference of means=0.174 µIU/mL, p=0.007, for the unadjusted analysis; difference of adjusted means=0.122 µIU/mL, p=0.036, for adjusted analysis). The adjusted mean TSH level for Ranch Hands in the background dioxin category was 1.682 µIU/mL versus 1.560 µIU/mL for the Comparisons.

No significant relation was seen between TSH in its continuous form and 1987 dioxin in either the unadjusted or adjusted Model 4 analyses (Table 18-12(g,h): p>0.40 for each analysis).

18.2.2.3.2 TSH (Discrete)

All unadjusted and adjusted analyses of TSH in its discrete form for Models 1 through 4 were nonsignificant (Table 18-13(a-h): p>0.09 for each analysis).

Table 18-12. Analysis of TSH (μIU/mL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*733*	*1.829*	*0.108*	*0.023**
	Comparison	*1,089*	*1.721*		
Officer	Ranch Hand	284	2.014	0.211	0.010**
	Comparison	419	1.803		
Enlisted Flyer	Ranch Hand	126	1.694	-0.104	0.362
	Comparison	174	1.797		
Enlisted Groundcrew	Ranch Hand	323	1.733	0.102	0.128
	Comparison	496	1.630		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*732*	*1.653*	*0.096*	*0.024**
	Comparison	*1,089*	*1.557*		
Officer	Ranch Hand	283	1.778	0.189	0.009**
	Comparison	419	1.589		
Enlisted Flyer	Ranch Hand	126	1.516	-0.094	0.354
	Comparison	174	1.610		
Enlisted Groundcrew	Ranch Hand	323	1.611	0.093	0.132
	Comparison	496	1.517		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Table 18-12. Analysis of TSH (µIU/mL) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	134	1.802	1.809	0.014	-0.012 (0.020)	0.541
Medium	139	1.825	1.833			
High	131	1.734	1.719			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of TSH versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	134	1.476	0.081	0.004 (0.023)	0.853
Medium	139	1.555			
High	131	1.496			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of TSH versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,089	1.721	1.721		
Background RH	328	1.885	1.895	0.174	0.007**
Low RH	201	1.801	1.797	0.076	0.316
High RH	203	1.775	1.764	0.043	0.564
Low plus High RH	404	1.788	1.781	0.060	0.300

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

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Table 18-12. Analysis of TSH (µIU/mL) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,089	1.560		
Background RH	327	1.682	0.122	0.036*
Low RH	201	1.614	0.054	0.422
High RH	203	1.656	0.096	0.172
Low plus High RH	404	1.635	0.075	0.150

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < $ p-value ≤ 0.050).

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
     Low (Ranch Hand): 1987 dioxin $>$ 10 ppt, 10 ppt $<$ initial dioxin $\leq$ 118 ppt.
     High (Ranch Hand): 1987 dioxin $>$ 10 ppt, initial dioxin $>$ 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	244	1.872	0.001	-0.010 (0.013)	0.405
Medium	244	1.896			
High	244	1.729			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of TSH versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = $>$7.8-19.2 ppt; High = $>$19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	243	1.558	0.064	-0.003 (0.014)	0.854
Medium	244	1.568			
High	244	1.488			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of TSH versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = $>$7.8–19.2 ppt; High = $>$19.2 ppt.

Table 18-13. Analysis of TSH (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal Unadjusted Relative Risk (95% C.I.)	p-Value	Abnormal High vs. Normal Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*733*	*1 (0.1)*	*710 (96.9)*	*22 (3.0)*	*0.21 (0.03,1.74)*	*0.149*	*1.49 (0.82,2.72)*	*0.189*
	Comparison	*1,089*	*7 (0.6)*	*1,060 (97.3)*	*22 (2.0)*				
Officer	Ranch Hand	284	0 (0.0)	274 (96.5)	10 (3.5)	--	0.405[a]	1.34 (0.56,3.21)	0.506
	Comparison	419	3 (0.7)	405 (96.7)	11 (2.6)				
Enlisted Flyer	Ranch Hand	126	1 (0.8)	122 (96.8)	3 (2.4)	1.39 (0.11,17.88)	0.799	1.39 (0.28,7.02)	0.688
	Comparison	174	1 (0.6)	170 (97.7)	3 (1.7)				
Enlisted Groundcrew	Ranch Hand	323	0 (0.0)	314 (97.2)	9 (2.8)	--	0.424[a]	1.74 (0.66,4.55)	0.261
	Comparison	496	3 (0.6)	485 (97.8)	8 (1.6)				

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormally low TSH.

--: Results were not presented because of the sparse number of participants with abnormally low TSH.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Abnormal Low vs. Normal Adjusted Relative Risk (95% C.I.)	p-Value	Abnormal High vs. Normal Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,821*	*0.21 (0.03,1.71)*	*0.144*	*1.49 (0.82,2.72)*	*0.190*
Officer	702	--	--	1.34 (0.56,3.20)	0.512
Enlisted Flyer	300	1.34 (0.10,17.22)	0.822	1.38 (0.27,6.96)	0.696
Enlisted Groundcrew	819	--	--	1.75 (0.67,4.59)	0.253

--: Results were not presented because of the sparse number of participants with abnormally low TSH.

Note: Results were not adjusted for race because of the sparse number of participants with abnormally low TSH.

Table 18-13. Analysis of TSH (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

| | | Initial Dioxin Category Summary Statistics Number (%) | | | Analysis Results for Log_2 (Initial Dioxin)[a] | | | | |
| | | | | | Abnormal Low vs. Normal | | Abnormal High vs. Normal | | |
Initial Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]	p-Value
Low	134	0 (0.0)	132 (98.5)	2 (1.5)	1.56 (0.44,5.57)	0.493	0.92 (0.56,1.51)	0.752
Medium	139	0 (0.0)	133 (95.7)	6 (4.3)				
High	131	1 (0.8)	128 (97.7)	2 (1.5)				

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

| | Analysis Results for Log_2 (Initial Dioxin) | | | | |
| | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
404	1.85 (0.48,7.20)	0.374	1.00 (0.60,1.66)	0.989

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with abnormally low TSH.

Table 18-13. Analysis of TSH (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,089	7 (0.6)	1,060 (97.3)	22 (2.0)				
Background RH	328	0 (0.0)	316 (96.3)	12 (3.7)	--	0.321[c]	1.84 (0.89,3.78)	0.098
Low RH	201	0 (0.0)	196 (97.5)	5 (2.5)	--	0.539[c]	1.23 (0.46,3.28)	0.683
High RH	203	1 (0.5)	197 (97.0)	5 (2.5)	0.76 (0.09,6.25)	0.796	1.22 (0.45,3.27)	0.697
Low plus High RH	404	1 (0.2)	393 (97.3)	10 (2.5)	--	0.600[c]	1.22 (0.57,2.61)	0.605

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

[b]Relative risk and confidence interval relative to Comparisons.

[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with an abnormally low TSH.

--: Results were not presented because of the sparse number of participants with abnormally low TSH.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-13. Analysis of TSH (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,089				
Background RH	327	--	--	1.71 (0.82,3.57)	0.152
Low RH	201	--	--	1.20 (0.45,3.24)	0.714
High RH	203	0.84 (0.09,7.63)	0.873	1.41 (0.50,3.95)	0.511
Low plus High RH	404	--	--	1.30 (0.60,2.82)	0.500

[a]Relative risk and confidence interval relative to Comparisons.
--: Results were not presented because of the sparse number of participants with abnormally low TSH.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Results were not adjusted for race because of the sparse number of participants with abnormally low TSH.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category	n	1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	244	0 (0.0)	235 (96.3)	9 (3.7)	1.92 (0.62,5.94)	0.256	0.91 (0.70,1.19)	0.494
Medium	244	0 (0.0)	238 (97.5)	6 (2.5)				
High	244	1 (0.4)	236 (96.7)	7 (2.9)				

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

Table 18-13. Analysis of TSH (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)				
	Abnormal Low vs. Normal			Abnormal High vs. Normal	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value		Adjusted Relative Risk (95% C.I.)[a]	p-Value
731	2.13 (0.72,6.30)	0.171		0.93 (0.70,1.24)	0.633

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with abnormally low TSH.

18.2.2.3.3 Free T$_4$ (Continuous)

The Model 1 unadjusted analysis of free T$_4$ in its continuous form revealed a significant mean difference between Ranch Hands and Comparisons over all military occupations, as well as within the enlisted flyer stratum (Table 18-14(a): difference of means=0.016 ng/dL, p=0.047, overall; difference of means=0.062 ng/dL, p=0.001, for enlisted flyer stratum). The adjusted Model 1 analysis of free T$_4$ showed no significant overall group differences (Table 18-14(b): p=0.056). After stratifying the adjusted analysis by military occupation, a significant difference between Ranch Hands and Comparisons was seen among enlisted flyers (Table 18-14(b): difference of adjusted means=0.061 ng/dL, p=0.002). A higher adjusted mean free T$_4$ level was seen among Ranch Hand enlisted flyers (1.115 ng/dL) than among Comparison enlisted flyers (1.054 ng/dL).

All unadjusted and adjusted analyses for free T$_4$ in Models 2, 3, and 4 were nonsignificant (Table 18-14(c-h): p≥0.09 for each analysis).

Table 18-14. Analysis of Free T$_4$ (ng/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*733*	*1.080*	*0.016*	*0.047**
	Comparison	*1,089*	*1.064*		
Officer	Ranch Hand	284	1.076	0.005	0.700
	Comparison	419	1.071		
Enlisted Flyer	Ranch Hand	126	1.116	0.062	0.001**
	Comparison	174	1.054		
Enlisted Groundcrew	Ranch Hand	323	1.069	0.007	0.531
	Comparison	496	1.062		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

 *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Table 18-14. Analysis of Free T$_4$ (ng/dL) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*732*	*1.081*	*0.015*	*0.056*
	Comparison	*1,089*	*1.066*		
Officer	Ranch Hand	283	1.072	0.003	0.788
	Comparison	419	1.068		
Enlisted Flyer	Ranch Hand	126	1.115	0.061	0.002**
	Comparison	174	1.054		
Enlisted Groundcrew	Ranch Hand	323	1.074	0.008	0.482
	Comparison	496	1.065		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

**: Statistically significant (p-value ≤ 0.010).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

	Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]		R^2	Slope (Standard Error)[b,c]	p-Value
Low	134	1.084	1.083		0.017	-0.005 (0.006)	0.392
Medium	139	1.077	1.076				
High	131	1.066	1.069				

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of free T$_4$ versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]		R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	134	1.102		0.040	-0.003 (0.006)	0.598
Medium	139	1.097				
High	131	1.091				

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of free T$_4$ versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 18-14. Analysis of Free T₄ (ng/dL) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,089	1.064	1.064		
Background RH	328	1.084	1.081	0.017	0.102
Low RH	201	1.075	1.076	0.012	0.342
High RH	203	1.077	1.080	0.016	0.215
Low plus High RH	404	1.076	1.078	0.014	0.150

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,089	1.066		
Background RH	327	1.080	0.014	0.191
Low RH	201	1.080	0.014	0.271
High RH	203	1.085	0.019	0.145
Low plus High RH	404	1.083	0.017	0.090

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-14. Analysis of Free T₄ (ng/dL) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	244	1.082	0.001	-0.003 (0.003)	0.441
Medium	244	1.083			
High	244	1.074			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of free T_4 versus $\log_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	243	1.086	0.030	0.001 (0.004)	0.775
Medium	244	1.097			
High	244	1.092			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of free T_4 versus $\log_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

18.2.2.3.4 Free T₄ (Discrete)

The unadjusted and adjusted Model 1 analyses of free T_4 in its discrete form revealed no overall group difference (Table 18-15 (a,b): p>0.37 for both analyses). After stratifying by military occupation, however, a significant decrease in the percentage of free T_4 abnormalities was seen between Ranch Hands and Comparisons in the enlisted flyer stratum (Table 18-15(a,b): Unadjusted RR=0.37, p=0.025; Adjusted RR=0.37, p=0.026). Among enlisted flyers, Comparisons had a higher percentage of low free T_4 values than Ranch Hands (13.8 and 5.6, respectively).

No significant associations were seen in the unadjusted and adjusted analyses of free T_4 in Models 2 through 4 (Table 18-15(c-h): p>0.21 for each analysis).

Table 18-15. Analysis of Free T$_4$ (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*733*	*67 (9.1)*	*0.87 (0.63,1.19)*	*0.384*
	Comparison	*1,089*	*113 (10.4)*		
Officer	Ranch Hand	284	29 (10.2)	1.21 (0.72,2.02)	0.468
	Comparison	419	36 (8.6)		
Enlisted Flyer	Ranch Hand	126	7 (5.6)	0.37 (0.15,0.88)	0.025*
	Comparison	174	24 (13.8)		
Enlisted Groundcrew	Ranch Hand	323	31 (9.6)	0.89 (0.56,1.42)	0.616
	Comparison	496	53 (10.7)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,821*	*0.87 (0.63,1.19)*	*0.373*
Officer	702	1.21 (0.72,2.03)	0.469
Enlisted Flyer	300	0.37 (0.15,0.89)	0.026*
Enlisted Groundcrew	819	0.88 (0.55,1.40)	0.585

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	134	12 (9.0)	0.98 (0.76,1.26)	0.857
Medium	139	14 (10.1)		
High	131	11 (8.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 18-15. Analysis of Free T₄ (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
404	1.00 (0.75,1.34)	0.998

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,089	113 (10.4)		
Background RH	328	30 (9.1)	0.91 (0.59,1.39)	0.666
Low RH	201	20 (10.0)	0.94 (0.57,1.55)	0.804
High RH	203	17 (8.4)	0.75 (0.44,1.29)	0.297
Low plus High RH	404	37 (9.2)	0.84 (0.57,1.24)	0.383

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,089		
Background RH	327	0.95 (0.62,1.47)	0.825
Low RH	201	0.90 (0.54,1.50)	0.695
High RH	203	0.71 (0.41,1.23)	0.219
Low plus High RH	404	0.80 (0.54,1.19)	0.270

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-15. Analysis of Free T₄ (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Low**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	244	26 (10.7)	0.99 (0.84,1.15)	0.864
Medium	244	19 (7.8)		
High	244	22 (9.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
731	0.94 (0.78,1.13)	0.511

[a]Relative risk for a twofold increase in 1987 dioxin.

18.2.2.3.5 Anti-thyroid Antibodies

All unadjusted and adjusted analyses of anti-thyroid antibodies were nonsignificant for Models 1 through 4 (Table 18-16(a-h): p>0.39 for each analysis).

Table 18-16. Analysis of Anti-thyroid Antibodies

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*733*	*4 (0.5)*	*0.99 (0.28,3.52)*	*0.988*
	Comparison	*1,089*	*6 (0.6)*		
Officer	Ranch Hand	284	2 (0.7)	0.98 (0.16,5.92)	0.985
	Comparison	419	3 (0.7)		
Enlisted Flyer	Ranch Hand	126	2 (1.6)	2.79 (0.25,31.12)	0.404
	Comparison	174	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	323	0 (0.0)	--	0.676[a]
	Comparison	496	2 (0.4)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of participants with anti-thyroid antibodies present.

--: Results were not presented because of the sparse number of participants with anti-thyroid antibodies present.

Table 18-16. Analysis of Anti-thyroid Antibodies (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,821*	*0.98 (0.27,3.49)*	*0.974*
Officer	702	0.99 (0.16,5.99)	0.994
Enlisted Flyer	300	2.84 (0.25,31.70)	0.396
Enlisted Groundcrew	819	--	--

--: Results were not presented because of the sparse number of participants with anti-thyroid antibodies present.

Note: Results were not adjusted for race because of the sparse number of participants with anti-thyroid antibodies present.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	134	1 (0.7)	0.75 (0.28,2.03)	0.548
Medium	139	2 (1.4)		
High	131	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
404	0.84 (0.30,2.33)	0.724

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with anti-thyroid antibodies present.

Table 18-16. Analysis of Anti-thyroid Antibodies (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,089	6 (0.6)		
Background RH	328	1 (0.3)	0.56 (0.07,4.74)	0.598
Low RH	201	2 (1.0)	1.80 (0.36,9.00)	0.474
High RH	203	1 (0.5)	0.87 (0.10,7.36)	0.901
Low plus High RH	404	3 (0.7)	1.25 (0.29,5.36)	0.762

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,089		
Background RH	327	0.47 (0.06,4.01)	0.492
Low RH	201	1.71 (0.34,8.68)	0.519
High RH	203	1.29 (0.14,12.19)	0.827
Low plus High RH	404	1.48 (0.33,6.68)	0.609

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Note: Results were not adjusted for race because of the sparse number of participants with anti-thyroid antibodies present.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	244	1 (0.4)	0.95 (0.51,1.76)	0.872
Medium	244	1 (0.4)		
High	244	2 (0.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 18-16. Analysis of Anti-thyroid Antibodies (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
731	1.02 (0.54,1.94)	0.953

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with anti-thyroid antibodies present.

18.2.2.3.6 Fasting Glucose (Continuous)

All unadjusted and adjusted analyses of fasting glucose in its continuous form were nonsignificant for Models 1 through 3 (Table 18-17(a-f): p>0.07 for each analysis).

The unadjusted Model 4 analysis revealed a significant positive relation between fasting glucose and 1987 dioxin (Table 18-17(g): Slope=0.016, p<0.001). After adjusting for covariates, however, the results were nonsignificant (Table 18-17(h): p=0.068).

Table 18-17. Analysis of Fasting Glucose (mg/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*776*	*101.7*	*-0.3*	*0.757*
	Comparison	*1,173*	*102.0*		
Officer	Ranch Hand	306	100.5	0.0	0.994
	Comparison	462	100.5		
Enlisted Flyer	Ranch Hand	133	102.6	-1.2	0.627
	Comparison	185	103.8		
Enlisted Groundcrew	Ranch Hand	337	102.6	-0.3	0.853
	Comparison	526	102.8		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 18-17. Analysis of Fasting Glucose (mg/dL) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*767*	*105.2*	*-0.1*	*0.942*
	Comparison	*1,162*	*105.2*		
Officer	Ranch Hand	303	104.1	-0.4	0.778
	Comparison	460	104.5		
Enlisted Flyer	Ranch Hand	130	105.0	0.3	0.906
	Comparison	181	104.7		
Enlisted Groundcrew	Ranch Hand	334	106.5	0.1	0.932
	Comparison	521	106.4		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	140	101.5	102.0	0.101	0.014 (0.008)	0.079
Medium	142	103.0	103.2			
High	141	105.9	105.1			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of fasting glucose versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	104.4	0.125	0.016 (0.009)	0.079
Medium	138	105.8			
High	140	107.5			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of fasting glucose versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 18-17. Analysis of Fasting Glucose (mg/dL) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,173	102.0	101.9		
Background RH	352	99.8	101.7	-0.2	0.834
Low RH	210	102.8	102.1	0.2	0.923
High RH	213	104.1	102.2	0.3	0.848
Low plus High RH	423	103.4	102.2	0.3	0.849

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,162	105.0		
Background RH	349	105.4	0.4	0.781
Low RH	206	105.1	0.1	0.984
High RH	211	105.4	0.4	0.792
Low plus High RH	417	105.3	0.3	0.848

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-17. Analysis of Fasting Glucose (mg/dL) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	260	98.8	0.016	0.016 (0.005)	<0.001**
Medium	258	101.7			
High	257	104.9			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of fasting glucose versus log_2 (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	257	103.6	0.095	0.010 (0.005)	0.068
Medium	257	103.9			
High	252	107.2			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of fasting glucose versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

18.2.2.3.7 Fasting Glucose (Discrete)

No significant associations were revealed in the unadjusted and adjusted Model 1 through 3 analyses of fasting glucose in its discrete form (Table 18-18(a-f): p>0.16 for each analysis).

The unadjusted Model 4 analysis showed a significant positive relation between fasting glucose in its discrete form and 1987 dioxin (Table 18-18(g): Unadjusted RR=1.12, p=0.032). After covariate adjustment the results became nonsignificant (Table 18-18(h): p=0.729).

Table 18-18. Analysis of Fasting Glucose (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*776*	*164 (21.1)*	*1.06 (0.85,1.33)*	*0.588*
	Comparison	*1,173*	*236 (20.1)*		
Officer	Ranch Hand	306	60 (19.6)	1.08 (0.75,1.56)	0.675
	Comparison	462	85 (18.4)		
Enlisted Flyer	Ranch Hand	133	30 (22.6)	0.93 (0.55,1.58)	0.798
	Comparison	185	44 (23.8)		
Enlisted Groundcrew	Ranch Hand	337	74 (22.0)	1.10 (0.79,1.54)	0.569
	Comparison	526	107 (20.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,929*	*1.09 (0.86,1.38)*	*0.469*
Officer	763	1.05 (0.71,1.54)	0.819
Enlisted Flyer	311	0.96 (0.55,1.68)	0.882
Enlisted Groundcrew	855	1.19 (0.84,1.70)	0.332

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	35 (25.0)	1.02 (0.86,1.22)	0.811
Medium	142	32 (22.5)		
High	141	35 (24.8)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	1.09 (0.88,1.35)	0.409

[a]Relative risk for a twofold increase in initial dioxin.

Table 18-18. Analysis of Fasting Glucose (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,173	236 (20.1)		
Background RH	352	62 (17.6)	1.05 (0.76,1.45)	0.775
Low RH	210	53 (25.2)	1.29 (0.90,1.85)	0.166
High RH	213	49 (23.0)	1.00 (0.69,1.45)	0.990
Low plus High RH	423	102 (24.1)	1.14 (0.86,1.50)	0.369

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,162		
Background RH	349	1.14 (0.81,1.59)	0.455
Low RH	206	1.25 (0.86,1.82)	0.238
High RH	211	1.03 (0.70,1.53)	0.869
Low plus High RH	417	1.14 (0.85,1.52)	0.388

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	44 (16.9)	1.12 (1.01,1.25)	0.032**
Medium	258	58 (22.5)		
High	257	62 (24.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 18-18. Analysis of Fasting Glucose (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
766	1.02 (0.89,1.18)	0.729

[a]Relative risk for a twofold increase in 1987 dioxin.

18.2.2.3.8 2-hour Postprandial Glucose (Nondiabetics Only) (Continuous)

No overall group differences were revealed in the unadjusted and adjusted Model 1 analyses of 2-hour postprandial glucose in its continuous form for nondiabetic participants (Table 18-19(a,b): p>0.45 for each analysis). After stratifying by military occupation, a significant group difference was revealed among enlisted groundcrew in the unadjusted and adjusted analyses (Table 18-19(a,b): difference of means=-6.7 mg/dL, p=0.013; difference of adjusted means=-7.4 mg/dL, p=0.006). Among the enlisted groundcrew, Ranch Hands had a mean 2-hour postprandial glucose value of 107.4 mg/dL versus 114.8 mg/dL for Comparisons.

All unadjusted and adjusted analyses of 2-hour postprandial glucose in its continuous form were nonsignificant for Models 2 through 4 (Table 18-19(c-h): p≥0.10 for each analysis).

Table 18-19. Analysis of 2-hour Postprandial Glucose (mg/dL) (Nondiabetics Only) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*629*	*106.5*	*-1.2*	*0.509*
	Comparison	*936*	*107.7*		
Officer	Ranch Hand	254	109.6	4.8	0.100
	Comparison	378	104.8		
Enlisted Flyer	Ranch Hand	102	114.0	-1.5	0.763
	Comparison	140	115.5		
Enlisted Groundcrew	Ranch Hand	273	101.0	-6.7	0.013*
	Comparison	418	107.8		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*623*	*111.4*	*-1.4*	*0.454*
	Comparison	*931*	*112.8*		
Officer	Ranch Hand	251	112.3	4.7	0.096
	Comparison	377	107.6		
Enlisted Flyer	Ranch Hand	101	115.2	0.0	0.999
	Comparison	139	115.2		
Enlisted Groundcrew	Ranch Hand	271	107.4	-7.4	0.006**
	Comparison	415	114.8		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

**: Statistically significant (p-value$\leq$0.010).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

	Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]		R^2	Slope (Standard Error)[b,c]	p-Value
Low	108	107.3	108.5		0.039	-0.020 (0.015)	0.176
Medium	107	109.1	109.5				
High	105	102.7	101.1				

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]		R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	107	108.4		0.137	0.000 (0.017)	0.997
Medium	105	111.7				
High	105	107.8				

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	936	107.7	107.5		
Background RH	308	106.6	108.0	0.5	0.832
Low RH	161	108.2	108.3	0.8	0.808
High RH	159	104.5	102.6	-4.9	0.102
Low plus High RH	320	106.4	105.4	-2.1	0.359

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	931	112.7		
Background RH	305	113.3	0.6	0.794
Low RH	158	109.6	-3.1	0.298
High RH	159	108.3	-4.4	0.153
Low plus High RH	317	108.9	-3.8	0.100

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	233	106.0	<0.001	-0.005 (0.009)	0.601
Medium	204	108.5			
High	191	105.0			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	230	112.8	0.126	-0.007 (0.010)	0.492
Medium	203	111.0			
High	189	112.3			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of 2-hour postprandial glucose versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

18.2.2.3.9 2-hour Postprandial Glucose (Nondiabetics Only) (Discrete)

The unadjusted and adjusted Model 1 analyses of 2-hour postprandial glucose in its discrete form on nondiabetic participants revealed no significant group differences (Table 18-20(a,b): p>0.17 for each analysis).

A significant association between 2-hour postprandial glucose and initial dioxin was revealed in the unadjusted Model 2 analysis (Table 18-20(c): Unadjusted RR=0.79, p=0.037). After adjusting for covariates, however, the results were nonsignificant (Table 18-20(d): p=0.094).

No significant associations were seen in the Model 3 and 4 unadjusted and adjusted analyses of 2-hour postprandial glucose (Table 18-20(e-h): p>0.09 for each analysis).

Table 18-20. Analysis of 2-hour Postprandial Glucose (Nondiabetics Only) (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Impaired	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*629*	*133 (21.1)*	*1.00 (0.78,1.28)*	*0.997*
	Comparison	*936*	*198 (21.2)*		
Officer	Ranch Hand	254	54 (21.3)	1.30 (0.87,1.94)	0.201
	Comparison	378	65 (17.2)		
Enlisted Flyer	Ranch Hand	102	28 (27.5)	0.98 (0.55,1.73)	0.944
	Comparison	140	39 (27.9)		
Enlisted Groundcrew	Ranch Hand	273	51 (18.7)	0.79 (0.54,1.16)	0.230
	Comparison	418	94 (22.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,554*	*1.00 (0.77,1.29)*	*0.992*
Officer	628	1.34 (0.88,2.03)	0.172
Enlisted Flyer	240	1.02 (0.56,1.83)	0.958
Enlisted Groundcrew	686	0.77 (0.52,1.15)	0.201

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Impaired	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	108	27 (25.0)	0.79 (0.63,0.99)	0.037*
Medium	107	29 (27.1)		
High	105	15 (14.3)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
317	0.80 (0.61,1.04)	0.094

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Impaired	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	936	198 (21.2)		
Background RH	308	62 (20.1)	1.00 (0.73,1.39)	0.980
Low RH	161	40 (24.8)	1.25 (0.84,1.85)	0.269
High RH	159	31 (19.5)	0.84 (0.55,1.28)	0.418
Low plus High RH	320	71 (22.2)	1.02 (0.75,1.40)	0.879

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	931		
Background RH	305	1.06 (0.75,1.49)	0.739
Low RH	158	1.06 (0.70,1.60)	0.772
High RH	159	0.78 (0.50,1.22)	0.280
Low plus High RH	317	0.91 (0.66,1.26)	0.570

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Impaired	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	233	47 (20.2)	0.96 (0.85,1.08)	0.470
Medium	204	47 (23.0)		
High	191	39 (20.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
622	0.88 (0.75,1.02)	0.091

[a]Relative risk for a twofold increase in 1987 dioxin.

18.2.2.3.10   2-hour Postprandial Urinary Glucose (Nondiabetics Only)

The unadjusted Model 1 analysis of 2-hour postprandial urinary glucose on nondiabetic participants showed no group differences (Table 18-21(a): p≥0.07 for each analysis). Adjusting for covariates in Model 1 showed no overall group differences (Table 18-21(b): p=0.583). Stratifying by military occupation, however, revealed a significant difference between Ranch Hands and Comparisons among officers (Table 18-21(b): Adjusted RR=1.48, p=0.050). Among officers, Ranch Hands had a higher prevalence of 2-hour postprandial urinary glucose than Comparisons did (23.6% versus 17.7%).

All results for the unadjusted and adjusted analyses of 2-hour postprandial urinary glucose for Models 2 and 3 were nonsignificant (Table 18-21(c-f): p>0.50 for each analysis).

No significant relation was seen between 1987 dioxin and 2-hour postprandial urinary glucose in the unadjusted Model 4 analysis (Table 18-21(g): p=0.660). After adjusting for covariates, however, the results became significant (Table 18-21(h): Adjusted RR=0.87, p=0.040). The percentages of Ranch Hands with 2-hour postprandial urinary glucose present were 27.9, 25.5, and 28.3 for the low, medium, and high 1987 dioxin categories, respectively.

Table 18-21. Analysis of 2-hour Postprandial Urinary Glucose (Nondiabetics Only)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*629*	*171 (27.2)*	*1.07 (0.85,1.35)*	*0.558*
	Comparison	*936*	*242 (25.9)*		
Officer	Ranch Hand	254	60 (23.6)	1.44 (0.97,2.12)	0.070
	Comparison	378	67 (17.7)		
Enlisted Flyer	Ranch Hand	102	33 (32.4)	1.01 (0.58,1.74)	0.972
	Comparison	140	45 (32.1)		
Enlisted Groundcrew	Ranch Hand	273	78 (28.6)	0.89 (0.63,1.24)	0.479
	Comparison	418	130 (31.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,554*	*1.07 (0.85,1.35)*	*0.583*
Officer	628	1.48 (1.00,2.20)	0.050*
Enlisted Flyer	240	1.02 (0.59,1.77)	0.940
Enlisted Groundcrew	686	0.86 (0.61,1.20)	0.367

*: Statistically significant ($0.010 < \text{p-value} \le 0.050$).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	108	21 (19.4)	1.07 (0.88,1.30)	0.502
Medium	107	35 (32.7)		
High	105	27 (25.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
317	1.05 (0.83,1.33)	0.678

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	936	242 (25.9)		
Background RH	308	88 (28.6)	1.14 (0.85,1.52)	0.370
Low RH	161	39 (24.2)	0.92 (0.62,1.35)	0.659
High RH	159	44 (27.7)	1.10 (0.76,1.61)	0.609
Low plus High RH	320	83 (25.9)	1.01 (0.75,1.34)	0.973

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	931		
Background RH	305	1.35 (1.00,1.82)	0.054
Low RH	158	0.84 (0.56,1.25)	0.388
High RH	159	0.82 (0.55,1.22)	0.333
Low plus High RH	317	0.83 (0.61,1.12)	0.224

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	233	65 (27.9)	0.98 (0.87,1.09)	0.660
Medium	204	52 (25.5)		
High	191	54 (28.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
622	0.87 (0.76,0.99)	0.040*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

18.2.2.3.11 Fasting Insulin (Continuous)

The unadjusted and adjusted Model 1 analyses of fasting insulin in its continuous form were nonsignificant (Table 18-22(a,b): $p \geq 0.16$ for each analysis).

Both the unadjusted and adjusted Model 2 analyses revealed significant positive relations between initial dioxin and fasting insulin (Table 18-22(c,d): Slope=0.047, p=0.030; Adjusted Slope=0.056, p=0.014). The adjusted mean fasting insulin levels in the low, medium, and high initial dioxin categories were 11.84 μIU/mL, 11.86 μIU/mL, and 13.01 μIU/mL, respectively.

The Model 3 unadjusted analysis revealed two significant contrasts: Ranch Hands in the high dioxin category versus Comparisons and Ranch Hands in the low and high dioxin categories combined versus Comparisons (Table 18-22(e): difference of means=1.21 μIU/mL, p=0.009; difference of means=0.96 μIU/mL, p=0.006, respectively). After covariate adjustment, all contrasts were nonsignificant (Table 18-22(f): p>0.23 for each contrast).

The unadjusted Model 4 analysis revealed a significant relation between 1987 dioxin and fasting insulin in its continuous form (Table 18-22(g): Slope=0.077, p<0.001). After adjusting for covariates, the results became nonsignificant (Table 18-22(h): p=0.349).

Table 18-22. Analysis of Fasting Insulin (μIU/mL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*776*	*11.16*	*0.35*	*0.239*
	Comparison	*1,173*	*10.81*		
Officer	Ranch Hand	306	10.38	0.53	0.219
	Comparison	462	9.85		
Enlisted Flyer	Ranch Hand	133	10.98	-0.63	0.400
	Comparison	185	11.61		
Enlisted Groundcrew	Ranch Hand	337	11.99	0.55	0.244
	Comparison	526	11.44		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*767*	*11.10*	*0.36*	*0.160*
	Comparison	*1,162*	*10.74*		
Officer	Ranch Hand	303	10.73	0.46	0.242
	Comparison	460	10.27		
Enlisted Flyer	Ranch Hand	130	10.83	-0.25	0.694
	Comparison	181	11.08		
Enlisted Groundcrew	Ranch Hand	334	11.53	0.50	0.212
	Comparison	521	11.03		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 18-22. Analysis of Fasting Insulin (μIU/mL) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	140	11.56	11.75	0.143	0.047 (0.021)	0.030*
Medium	142	11.98	12.08			
High	141	13.19	12.87			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of fasting insulin versus log_2 (initial dioxin).

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	11.84	0.322	0.056 (0.023)	0.014*
Medium	138	11.86			
High	140	13.01			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of fasting insulin versus log_2 (initial dioxin).

*: Statistically significant ($0.010 < \text{p-value} \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 18-22. Analysis of Fasting Insulin (μIU/mL) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,173	10.81	10.77		
Background RH	352	10.05	10.69	-0.08	0.809
Low RH	210	11.74	11.49	0.72	0.113
High RH	213	12.72	11.98	1.21	0.009**
Low plus High RH	423	12.23	11.73	0.96	0.006**

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,162	10.77		
Background RH	349	11.07	0.30	0.379
Low RH	206	11.03	0.26	0.528
High RH	211	11.27	0.50	0.247
Low plus High RH	417	11.15	0.38	0.233

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-22. Analysis of Fasting Insulin (µIU/mL) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	260	9.80	0.040	0.077 (0.014)	<0.001**
Medium	258	11.19			
High	257	12.79			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of fasting insulin versus log_2 (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	257	11.35	0.307	0.013 (0.014)	0.349
Medium	257	11.06			
High	252	11.50			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of fasting insulin versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

18.2.2.3.12 *Fasting Insulin (Discrete)*

A significant difference in the percentage of participants with abnormally high fasting insulin levels was observed between Ranch Hands and Comparisons in the unadjusted Model 1 analysis (Table 18-23(a): Unadjusted RR=1.45, p=0.046). After adjusting for covariates, the results became nonsignificant (Table 18-23(b): p=0.072). No significant associations were seen in the unadjusted and adjusted analyses after stratifying by military occupation (Table 18-23(a,b): p>0.05 for each analysis).

Both the unadjusted and adjusted Model 2 analysis revealed a significant positive association between initial dioxin and abnormally high fasting insulin levels (Table 18-23(c,d): Unadjusted RR=1.31, p=0.019; Adjusted RR=1.54, p=0.006). The percentages of Ranch Hands with abnormally high fasting insulin levels in the low, medium, and high initial dioxin categories were 6.4, 9.9, and 13.5, respectively.

Two significant contrasts were revealed in the Model 3 unadjusted analysis of abnormally high fasting insulin (Table 18-23(e): Unadjusted RR=1.96, p=0.009 for Ranch Hands in the high dioxin category versus Comparisons; Unadjusted RR=1.67, p=0.018 for Ranch Hands in the low and high dioxin categories combined versus Comparisons). After adjusting for covariates, the results became nonsignificant (Table 18-23(f): p>0.07 for each contrast).

The unadjusted Model 4 analysis revealed a significant inverse association between 1987 dioxin and abnormally low fasting insulin levels, as well as a significant positive association between 1987 dioxin and abnormally high fasting insulin levels (Table 18-23(g): Unadjusted RR=0.76, p=0.002; Unadjusted RR=1.34, p<0.001, respectively). After covariate adjustment, however, these relations became nonsignificant (Table 18-23(h): p>0.09 for each analysis).

18.2.2.3.13   2-hour Postprandial Insulin (Nondiabetics Only) (Continuous)

The unadjusted Model 1 analysis of 2-hour postprandial insulin in its continuous form for nondiabetic participants did not show a significant group difference overall or after stratifying by military occupation (Table 18-24(a): p≥0.09 for each analysis). After adjusting for covariates, the difference in mean 2-hour postprandial insulin levels between all Ranch Hands and Comparisons was not significant, and no significant difference was seen between Ranch Hands and Comparisons in the officer or enlisted flyer strata (Table 18-24(b): p>0.34 for each analysis). A significant difference in mean 2-hour postprandial insulin level was seen, however, between Ranch Hands and Comparisons within the enlisted groundcrew stratum (Table 18-24(b): difference of adjusted means=-7.64 µIU/mL, p=0.033). Among the enlisted groundcrew, Ranch Hands had a mean 2-hour postprandial insulin level of 61.83 µIU/mL versus 69.47 µIU/mL for Comparisons.

The Model 2 and 3 unadjusted and adjusted analyses of 2-hour postprandial insulin revealed no significant results (Table 18-24(c-f): p>0.16 for each analysis).

A significant positive association was revealed between 1987 dioxin and the 2-hour postprandial insulin in the unadjusted Model 4 analysis (Table 18-24(g): Slope=0.058, p=0.004). After adjusting for covariates, however, the results became nonsignificant (Table 18-24(h): p=0.937).

Table 18-23. Analysis of Fasting Insulin (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
			Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)	p-Value	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*776*	*64 (8.2)*	*652 (84.0)*	*60 (7.7)*	*0.84 (0.61,1.16)*	*0.290*	*1.45 (1.01,2.10)*	*0.046**
	Comparison	*1,173*	*116 (9.9)*	*994 (84.7)*	*63 (5.4)*				
Officer	Ranch Hand	306	34 (11.1)	253 (82.7)	19 (6.2)	1.02 (0.64,1.61)	0.947	1.74 (0.89,3.40)	0.108
	Comparison	462	52 (11.3)	393 (85.1)	17 (3.7)				
Enlisted Flyer	Ranch Hand	133	9 (6.8)	117 (88.0)	7 (5.3)	0.81 (0.34,1.90)	0.621	0.72 (0.28,1.87)	0.502
	Comparison	185	15 (8.1)	157 (84.9)	13 (7.0)				
Enlisted Groundcrew	Ranch Hand	337	21 (6.2)	282 (83.7)	34 (10.1)	0.67 (0.40,1.15)	0.148	1.62 (0.98,2.68)	0.059
	Comparison	526	49 (9.3)	444 (84.4)	33 (6.3)				

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Adjusted Relative Risk (95% C.I.)	p-Value	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,929*	*0.77 (0.54,1.08)*	*0.127*	*1.43 (0.97,2.10)*	*0.072*
Officer	763	1.01 (0.62,1.64)	0.970	1.64 (0.82,3.28)	0.163
Enlisted Flyer	311	0.56 (0.22,1.45)	0.234	0.61 (0.21,1.72)	0.349
Enlisted Groundcrew	855	0.60 (0.34,1.06)	0.077	1.67 (0.98,2.83)	0.059

Table 18-23. Analysis of Fasting Insulin (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category	n	Initial Dioxin Category Summary Statistics Number (%)			Analysis Results for Log$_2$ (Initial Dioxin)[a]			
					Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]	p-Value
Low	140	11 (7.9)	120 (85.7)	9 (6.4)	0.79 (0.55,1.14)	0.209	1.31 (1.05,1.65)	0.019*
Medium	142	10 (7.0)	118 (83.1)	14 (9.9)				
High	141	4 (2.8)	118 (83.7)	19 (13.5)				

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log$_2$ (Initial Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	0.77 (0.49,1.20)	0.246	1.54 (1.13,2.09)	0.006**

[a]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Table 18-23. Analysis of Fasting Insulin (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Abnormal High vs. Normal Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,173	116 (9.9)	994 (84.7)	63 (5.4)				
Background RH	352	38 (10.8)	296 (84.1)	18 (5.1)	0.89 (0.59,1.32)	0.549	1.16 (0.67,2.02)	0.588
Low RH	210	16 (7.6)	177 (84.3)	17 (8.1)	0.79 (0.45,1.37)	0.398	1.42 (0.80,2.52)	0.233
High RH	213	9 (4.2)	179 (84.0)	25 (11.7)	0.51 (0.25,1.02)	0.058	1.96 (1.18,3.24)	0.009**
Low plus High RH	423	25 (5.9)	356 (84.2)	42 (9.9)	0.63 (0.39,1.01)	0.055	1.67 (1.09,2.55)	0.018*

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Abnormal Low vs. Normal Adjusted Relative Risk (95% C.I.)[a]	p-Value	Abnormal High vs. Normal Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,162				
Background RH	349	0.81 (0.53,1.22)	0.309	1.32 (0.74,2.35)	0.341
Low RH	206	0.85 (0.47,1.55)	0.598	1.26 (0.69,2.29)	0.449
High RH	211	0.54 (0.25,1.14)	0.105	1.64 (0.95,2.82)	0.076
Low plus High RH	417	0.67 (0.41,1.11)	0.123	1.44 (0.92,2.24)	0.107

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-23. Analysis of Fasting Insulin (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics					Analysis Results for Log$_2$ (1987 Dioxin)[a]			
		Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	260	31 (11.9)	217 (83.5)	12 (4.6)	0.76 (0.64,0.91)	0.002**	1.34 (1.14,1.58)	<0.001**
Medium	258	20 (7.8)	222 (86.0)	16 (6.2)				
High	257	12 (4.7)	213 (82.9)	32 (12.5)				

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)			
	Abnormal Low vs. Normal		Abnormal High vs. Normal	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
766	1.01 (0.82,1.25)	0.909	1.21 (0.97,1.51)	0.091

[a]Relative risk for a twofold increase in 1987 dioxin.

Table 18-24. Analysis of 2-hour Postprandial Insulin (μIU/mL) (Nondiabetics Only) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*629*	*57.77*	*-1.07*	*0.647*
	Comparison	*936*	*58.83*		
Officer	Ranch Hand	254	54.23	3.41	0.298
	Comparison	378	50.82		
Enlisted Flyer	Ranch Hand	102	66.41	-0.36	0.956
	Comparison	140	66.77		
Enlisted Groundcrew	Ranch Hand	273	58.16	-6.22	0.090
	Comparison	418	64.38		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*623*	*63.22*	*-1.37*	*0.554*
	Comparison	*931*	*64.60*		
Officer	Ranch Hand	251	60.15	3.18	0.342
	Comparison	377	56.97		
Enlisted Flyer	Ranch Hand	101	69.76	3.37	0.589
	Comparison	139	66.38		
Enlisted Groundcrew	Ranch Hand	271	61.83	-7.64	0.033*
	Comparison	415	69.47		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Table 18-24. *Analysis of 2-hour Postprandial Insulin (μIU/mL) (Nondiabetics Only) (Continuous) (Continued)*

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	108	58.90	60.96	0.067	0.032 (0.034)	0.352
Medium	107	63.18	63.91			
High	105	65.47	62.45			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of 2-hour postprandial insulin versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	107	63.98	0.226	0.052 (0.037)	0.163
Medium	105	64.84			
High	105	70.05			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of 2-hour postprandial insulin versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	936	58.83	58.56		
Background RH	308	53.45	55.88	-2.68	0.342
Low RH	161	61.03	61.11	2.55	0.505
High RH	159	63.87	60.12	1.56	0.684
Low plus High RH	320	62.43	60.62	2.06	0.477

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	931	64.52		
Background RH	305	64.00	-0.52	0.864
Low RH	158	61.27	-3.25	0.392
High RH	159	61.06	-3.46	0.376
Low plus High RH	317	61.16	-3.36	0.248

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	233	52.42	0.013	0.058 (0.020)	0.004**
Medium	204	58.22			
High	191	64.80			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of -hour postprandial insulin versus log_2 (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	230	67.57	0.222	-0.002 (0.022)	0.937
Medium	203	63.41			
High	189	67.41			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of -hour postprandial insulin versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

18.2.2.3.14   2-hour Postprandial Insulin (Nondiabetics Only) (Discrete)

No significant results were revealed in the unadjusted Model 1 analysis of 2-hour postprandial insulin in its discrete form for nondiabetic participants (Table 18-25(a): p>0.10 for each contrast). After covariate adjustment, a significant difference in the percentage of abnormally high 2-hour postprandial insulin levels was seen between Ranch Hands and Comparisons within the enlisted groundcrew stratum (Table 18-25(b): Adjusted RR=0.70, p=0.043). Among enlisted groundcrew, the percentage of participants with abnormally high 2-hour postprandial insulin levels was 49.1 percent for Ranch Hands versus 56.2 percent for Comparisons. All other contrasts were nonsignificant in the adjusted analysis (Table 18-25(b): p>0.32 for each contrast).

All results of the unadjusted and adjusted Model 2 and 3 analyses of 2-hour postprandial insulin in its discrete form were nonsignificant (Table 18-25(c-f): p>0.11 for each analysis).

A significant positive relation was seen between 1987 dioxin and abnormally high 2-hour postprandial insulin in the unadjusted Model 4 analysis (Table 18-25(g): Unadjusted RR=1.15, p=0.009). After covariate adjustment, however, all contrasts were nonsignificant (Table 18-25(h): p>0.66 for each contrast).

18.2.2.3.15   Hemoglobin A1c (Diabetics Only) (Continuous)

No significant differences in mean hemoglobin A1c values in diabetic participants were seen between exposure groups in Model 1 unadjusted and adjusted analyses (Table 18-26(a,b): p>0.45 for each analysis).

The unadjusted Model 2 analysis revealed a significant positive association between initial dioxin and hemoglobin A1c in its continuous form (Table 18-26(c): Slope=0.032, p=0.014). After adjusting for covariates, the results were no longer significant (Table 18-26(d): p=0.358). The unadjusted and adjusted Model 3 analyses revealed no significant contrasts (Table 18-26(e,f): p>0.23 for each analysis).

A significant positive relation was seen between 1987 dioxin and hemoglobin A1c in the unadjusted Model 4 analysis (Table 18-26(g): Slope=0.023, p=0.023). After adjusting for covariates, however, the results became nonsignificant (Table 18-26(h): p=0.095).

Table 18-25. Analysis of 2-hour Postprandial Insulin (Nondiabetics Only) (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%)			Abnormal Low vs. Normal		Abnormal High vs. Normal	
			Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)	p-Value	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*629*	*36 (5.7)*	*288 (45.8)*	*305 (48.5)*	*1.19 (0.75,1.90)*	*0.457*	*0.94 (0.77,1.16)*	*0.576*
	Comparison	*936*	*44 (4.7)*	*420 (44.9)*	*472 (50.4)*				
Officer	Ranch Hand	254	16 (6.3)	124 (48.8)	114 (44.9)	1.17 (0.59,2.32)	0.646	1.18 (0.85,1.64)	0.328
	Comparison	378	22 (5.8)	200 (52.9)	156 (41.3)				
Enlisted Flyer	Ranch Hand	102	3 (2.9)	42 (41.2)	57 (55.9)	0.98 (0.21,4.63)	0.982	0.92 (0.54,1.56)	0.760
	Comparison	140	4 (2.9)	55 (39.3)	81 (57.9)				
Enlisted Groundcrew	Ranch Hand	273	17 (6.2)	122 (44.7)	134 (49.1)	1.28 (0.63,2.58)	0.495	0.77 (0.56,1.06)	0.107
	Comparison	418	18 (4.3)	165 (39.5)	235 (56.2)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Adjusted Relative Risk (95% C.I.)	p-Value	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,554*	*1.27 (0.79,2.04)*	*0.324*	*0.93 (0.74,1.16)*	*0.533*
Officer	628	1.28 (0.64,2.57)	0.480	1.19 (0.84,1.69)	0.336
Enlisted Flyer	240	0.92 (0.19,4.38)	0.912	1.07 (0.61,1.89)	0.806
Enlisted Groundcrew	686	1.33 (0.65,2.71)	0.438	0.70 (0.50,0.99)	0.043*

*: Statistically significant (0.010<p-value≤0.050).

Table 18-25. Analysis of 2-hour Postprandial Insulin (Nondiabetics Only) (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category	n	Initial Dioxin Category Summary Statistics Number (%)			Analysis Results for Log_2 (Initial Dioxin)[a]			
					Abnormal Low vs. Normal		Abnormal High vs. Normal	
		Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]	p-Value
Low	108	4 (3.7)	51 (47.2)	53 (49.1)	1.16 (0.74,1.80)	0.514	1.10 (0.91,1.32)	0.333
Medium	107	1 (0.9)	51 (47.7)	55 (51.4)				
High	105	8 (7.6)	35 (33.3)	62 (59.0)				

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)				
	Abnormal Low vs. Normal		Abnormal High vs. Normal		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value	
317	1.12 (0.68,1.84)	0.661	1.18 (0.96,1.46)	0.116	

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for military occupation because of the sparse number of nondiabetic Ranch Hands with abnormally low 2-hour postprandial insulin values.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal Low	Number (%) Normal	Number (%) Abnormal High	Abnormal Low vs. Normal Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Abnormal High vs. Normal Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	936	44 (4.7)	420 (44.9)	472 (50.4)				
Background RH	308	23 (7.5)	150 (48.7)	135 (43.8)	1.38 (0.80,2.36)	0.249	0.88 (0.67,1.16)	0.370
Low RH	161	5 (3.1)	73 (45.3)	83 (51.6)	0.65 (0.25,1.71)	0.385	1.03 (0.73,1.46)	0.875
High RH	159	8 (5.0)	64 (40.3)	87 (54.7)	1.32 (0.59,2.94)	0.501	1.07 (0.75,1.53)	0.703
Low plus High RH	320	13 (4.1)	137 (42.8)	170 (53.1)	0.93 (0.48,1.80)	0.820	1.05 (0.80,1.37)	0.721

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Abnormal Low vs. Normal Adjusted Relative Risk (95% C.I.)[a]	p-Value	Abnormal High vs. Normal Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	931				
Background RH	305	1.45 (0.83,2.54)	0.187	0.98 (0.73,1.31)	0.884
Low RH	158	0.79 (0.30,2.09)	0.631	0.82 (0.56,1.19)	0.299
High RH	159	1.30 (0.55,3.07)	0.547	0.87 (0.59,1.29)	0.494
Low plus High RH	317	1.01 (0.51,2.01)	0.970	0.85 (0.63,1.13)	0.254

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-25. *Analysis of 2-hour Postprandial Insulin (Nondiabetics Only) (Discrete) (Continued)*

(g) MODEL 4: RANCH HANDS − 1987 DIOXIN − UNADJUSTED

| | | 1987 Dioxin Category Summary Statistics | | | Analysis Results for Log$_2$ (1987 Dioxin)[a] | | | |
| | | | Number (%) | | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
1987 Dioxin Category	n	Abnormal Low	Normal	Abnormal High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	233	20 (8.6)	113 (48.5)	100 (42.9)	0.91 (0.73,1.15)	0.440	1.15 (1.04,1.28)	0.009**
Medium	204	8 (3.9)	97 (47.5)	99 (48.5)				
High	191	8 (4.2)	77 (40.3)	106 (55.5)				

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS − 1987 DIOXIN − ADJUSTED

| | Analysis Results for Log$_2$ (1987 Dioxin) | | | |
| | Abnormal Low vs. Normal | | Abnormal High vs. Normal | |
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
622	0.94 (0.72,1.23)	0.668	1.02 (0.89,1.17)	0.777

[a]Relative risk for a twofold increase in 1987 dioxin.

Table 18-26. Analysis of Hemoglobin A1c (percent) (Diabetics Only) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*139*	*6.68*	*0.01*	*0.962*
	Comparison	*221*	*6.67*		
Officer	Ranch Hand	50	6.34	-0.08	0.706
	Comparison	76	6.42		
Enlisted Flyer	Ranch Hand	28	6.81	0.17	0.595
	Comparison	42	6.64		
Enlisted Groundcrew	Ranch Hand	61	6.91	0.03	0.870
	Comparison	103	6.88		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*136*	*6.95*	*0.06*	*0.674*
	Comparison	*215*	*6.89*		
Officer	Ranch Hand	50	6.69	-0.05	0.821
	Comparison	75	6.74		
Enlisted Flyer	Ranch Hand	26	7.05	0.25	0.454
	Comparison	39	6.80		
Enlisted Groundcrew	Ranch Hand	60	7.14	0.08	0.732
	Comparison	101	7.07		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	29	6.54	6.53	0.063	0.032 (0.013)	0.014*
Medium	34	6.73	6.73			
High	34	7.02	7.03			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of hemoglobin A1c versus log_2 (initial dioxin).

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	29	6.75	0.136	0.015 (0.016)	0.358
Medium	32	6.73			
High	33	6.80			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of hemoglobin A1c versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	221	6.67	6.67		
Background RH	42	6.47	6.50	-0.17	0.418
Low RH	46	6.60	6.58	-0.09	0.661
High RH	51	6.92	6.92	0.25	0.235
Low plus High RH	97	6.77	6.76	0.09	0.605

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	215	6.89		
Background RH	42	6.78	-0.11	0.626
Low RH	45	6.99	0.10	0.649
High RH	49	7.05	0.16	0.440
Low plus High RH	94	7.02	0.13	0.415

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	25	6.55	0.037	0.023 (0.010)	0.023*
Medium	50	6.46			
High	64	6.91			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of hemoglobin A1c versus log_2 (1987 dioxin).

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: Low = ≤ 7.8 ppt; Medium = $>7.8\text{-}19.2$ ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	25	6.81	0.115	0.019 (0.011)	0.095
Medium	50	6.80			
High	61	7.11			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of hemoglobin A1c versus log_2 (1987 dioxin).

Note: Low = ≤ 7.8 ppt; Medium = $>7.8\text{–}19.2$ ppt; High = >19.2 ppt.

18.2.2.3.16   Hemoglobin A1c (Diabetics Only) (Discrete)

Both the unadjusted and adjusted Model 1 analyses of hemoglobin A1c in its discrete form showed no significant group differences for diabetic participants (Table 18-27(a,b): p>0.50 for each analysis).

A significant positive association was seen between initial dioxin and hemoglobin A1c in the unadjusted Model 2 analysis (Table 18-27(c): Unadjusted RR=1.51, p=0.017). After adjusting for covariates, the results were no longer significant (Table 18-27(d): p=0.060).

No significant associations between hemoglobin A1c and categorized dioxin were revealed in the unadjusted and adjusted Model 3 analyses (Table 18-27(e,f): p>0.12 for each contrast).

The unadjusted and adjusted Model 4 analyses each showed a significant positive relation between 1987 dioxin and hemoglobin A1c in its discrete form (Table 18-27(g): Unadjusted RR=1.38, p=0.005; Adjusted RR=1.35, p=0.031). The percentages of participants with abnormally high hemoglobin A1c values in the low, medium, and high 1987 dioxin categories were 48.0, 62.0, and 73.4, respectively.

Table 18-27. Analysis of Hemoglobin A1c (Diabetics Only) (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*139*	*90 (64.7)*	*0.94 (0.60,1.47)*	*0.798*
	Comparison	*221*	*146 (66.1)*		
Officer	Ranch Hand	50	27 (54.0)	0.85 (0.42,1.75)	0.666
	Comparison	76	44 (57.9)		
Enlisted Flyer	Ranch Hand	28	18 (64.3)	0.81 (0.29,2.22)	0.678
	Comparison	42	29 (69.0)		
Enlisted Groundcrew	Ranch Hand	61	45 (73.8)	1.16 (0.57,2.35)	0.690
	Comparison	103	73 (70.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*351*	*0.97 (0.61,1.54)*	*0.907*
Officer	125	0.84 (0.41,1.74)	0.644
Enlisted Flyer	65	0.73 (0.25,2.13)	0.560
Enlisted Groundcrew	161	1.28 (0.61,2.68)	0.507

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	29	18 (62.1)	1.51 (1.05,2.19)	0.017*
Medium	34	23 (67.6)		
High	34	27 (79.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
94	1.51 (0.96,2.36)	0.060

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	221	146 (66.1)		
Background RH	42	22 (52.4)	0.59 (0.30,1.16)	0.129
Low RH	46	30 (65.2)	0.92 (0.47,1.80)	0.808
High RH	51	38 (74.5)	1.48 (0.74,2.96)	0.264
Low plus High RH	97	68 (70.1)	1.18 (0.70,1.99)	0.530

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	215		
Background RH	42	0.68 (0.34,1.36)	0.271
Low RH	45	1.03 (0.51,2.10)	0.929
High RH	49	1.33 (0.64,2.77)	0.445
Low plus High RH	94	1.18 (0.68,2.03)	0.554

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	25	12 (48.0)	1.38 (1.08,1.75)	0.005**
Medium	50	31 (62.0)		
High	64	47 (73.4)		

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
136	1.35 (1.01,1.80)	0.031*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

18.2.2.3.17   C-peptide (Diabetics Only) (Continuous)

All unadjusted and adjusted analyses of C-peptide in its continuous form for diabetic participants were nonsignificant for Models 1, 3, and 4 (Table 18-28(a,b,e-h): p>0.10 for each analysis).

Significant inverse associations were seen between initial dioxin and C-peptide in both the unadjusted and adjusted Model 2 analyses (Table 18-28(c,d): Slope=-0.088, p=0.007; Adjusted Slope=-0.091, p=0.017). The adjusted mean C-peptide values in the low, medium, and high initial dioxin categories were 3.69 ng/mL, 4.17 ng/mL, and 2.88 ng/mL, respectively.

Table 18-28. Analysis of C-peptide (ng/mL) (Diabetics Only) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*139*	*3.80*	*0.02*	*0.900*
	Comparison	*221*	*3.77*		
Officer	Ranch Hand	50	4.04	0.40	0.236
	Comparison	76	3.64		
Enlisted Flyer	Ranch Hand	28	3.44	-0.44	0.313
	Comparison	42	3.89		
Enlisted Groundcrew	Ranch Hand	61	3.77	-0.06	0.852
	Comparison	103	3.82		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*136*	*3.41*	*0.02*	*0.892*
	Comparison	*215*	*3.39*		
Officer	Ranch Hand	50	3.49	0.24	0.406
	Comparison	75	3.25		
Enlisted Flyer	Ranch Hand	26	3.27	-0.18	0.648
	Comparison	39	3.45		
Enlisted Groundcrew	Ranch Hand	60	3.45	-0.06	0.805
	Comparison	101	3.51		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	29	4.28	4.18	0.165	-0.088 (0.032)	0.007**
Medium	34	4.60	4.60			
High	34	3.13	3.21			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of C-peptide versus log_2 (initial dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	29	3.69	0.329	-0.091 (0.038)	0.017*
Medium	32	4.17			
High	33	2.88			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of C-peptide versus log_2 (initial dioxin).

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 18-28. Analysis of C-peptide (ng/mL) (Diabetics Only) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	221	3.77	3.78		
Background RH	42	3.42	3.63	-0.15	0.599
Low RH	46	4.44	4.25	0.47	0.108
High RH	51	3.56	3.50	-0.28	0.292
Low plus High RH	97	3.96	3.85	0.07	0.754

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	215	3.38		
Background RH	42	3.39	0.01	0.955
Low RH	45	3.76	0.38	0.158
High RH	49	3.10	-0.28	0.271
Low plus High RH	94	3.41	0.03	0.868

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	25	3.25	<0.001	0.000 (0.026)	0.998
Medium	50	4.15			
High	64	3.75			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of C-peptide versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	25	3.21	0.252	-0.014 (0.027)	0.598
Medium	50	3.66			
High	61	3.38			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of C-peptide versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

18.2.2.3.18 C-peptide (Diabetics Only) (Discrete)

All unadjusted and adjusted Model 1 through 4 analyses of C-peptide in its discrete form for diabetic participants were nonsignificant (Table 18-29(a-h): p>0.06 for each analysis).

Table 18-29. Analysis of C-peptide (Diabetics Only) (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*139*	*36 (25.9)*	*1.03 (0.63,1.67)*	*0.906*
	Comparison	*221*	*56 (25.3)*		
Officer	Ranch Hand	50	15 (30.0)	1.90 (0.82,4.39)	0.134
	Comparison	76	14 (18.4)		
Enlisted Flyer	Ranch Hand	28	4 (14.3)	0.42 (0.12,1.46)	0.171
	Comparison	42	12 (28.6)		
Enlisted Groundcrew	Ranch Hand	61	17 (27.9)	0.94 (0.47,1.90)	0.863
	Comparison	103	30 (29.1)		

Table 18-29. Analysis of C-peptide (Diabetics Only) (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*351*	*1.04 (0.61,1.80)*	*0.875*
Officer	125	1.63 (0.65,4.07)	0.295
Enlisted Flyer	65	0.53 (0.13,2.21)	0.381
Enlisted Groundcrew	161	0.94 (0.42,2.06)	0.868

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	29	9 (31.0)	0.73 (0.52,1.04)	0.068
Medium	34	14 (41.2)		
High	34	5 (14.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
94	0.63 (0.37,1.07)	0.067

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	221	56 (25.3)		
Background RH	42	8 (19.0)	0.82 (0.35,1.90)	0.643
Low RH	46	17 (37.0)	1.49 (0.75,2.99)	0.256
High RH	51	11 (21.6)	0.73 (0.34,1.56)	0.416
Low plus High RH	97	28 (28.9)	1.03 (0.58,1.80)	0.931

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-29. Analysis of C-peptide (Diabetics Only) (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	215		
Background RH	42	1.12 (0.45,2.80)	0.807
Low RH	45	1.63 (0.73,3.65)	0.231
High RH	49	0.68 (0.30,1.54)	0.356
Low plus High RH	94	1.03 (0.56,1.92)	0.914

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	25	5 (20.0)	0.97 (0.77,1.22)	0.812
Medium	50	14 (28.0)		
High	64	17 (26.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
136	0.85 (0.62,1.17)	0.324

[a]Relative risk for a twofold increase in 1987 dioxin.

18.2.2.3.19   Proinsulin (Diabetics Only) (Continuous)

No significant associations were revealed in the unadjusted and adjusted Model 1 through 4 analyses of proinsulin in its continuous form for diabetic participants (Table 18-30(a-h): p>0.17 for each analysis).

Table 18-30. Analysis of Proinsulin (pmol/L) (Diabetics Only) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*139*	*24.44*	*1.07*	*0.719*
	Comparison	*221*	*23.37*		
Officer	Ranch Hand	50	21.38	1.08	0.805
	Comparison	76	20.30		
Enlisted Flyer	Ranch Hand	28	26.33	2.08	0.770
	Comparison	42	24.25		
Enlisted Groundcrew	Ranch Hand	61	26.35	0.82	0.866
	Comparison	103	25.54		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*136*	*22.89*	*0.46*	*0.862*
	Comparison	*215*	*22.43*		
Officer	Ranch Hand	50	19.34	-0.34	0.929
	Comparison	75	19.68		
Enlisted Flyer	Ranch Hand	26	25.13	0.69	0.919
	Comparison	39	24.44		
Enlisted Groundcrew	Ranch Hand	60	24.60	1.14	0.787
	Comparison	101	23.46		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	29	27.12	25.75	0.073	-0.089 (0.080)	0.268
Medium	34	36.85	36.96			
High	34	23.26	24.24			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of proinsulin versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	29	24.20	0.155	-0.136 (0.100)	0.178
Medium	32	36.10			
High	33	21.03			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of proinsulin versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	221	23.37	23.51		
Background RH	42	16.98	19.30	-4.21	0.292
Low RH	46	29.01	26.11	2.60	0.560
High RH	51	28.26	27.26	3.75	0.388
Low plus High RH	97	28.62	26.71	3.20	0.345

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-30. Analysis of Proinsulin (pmol/L) (Diabetics Only) (Continuous) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	215	22.44		
Background RH	42	20.50	-1.94	0.628
Low RH	45	24.34	1.90	0.654
High RH	49	23.81	1.37	0.733
Low plus High RH	94	24.06	1.62	0.604

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	25	13.66	0.013	0.086 (0.064)	0.180
Medium	50	27.73			
High	64	27.79			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of proinsulin versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	25	18.74	0.196	-0.001 (0.071)	0.993
Medium	50	26.09			
High	61	25.16			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of proinsulin versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

18.2.2.3.20   Proinsulin (Diabetics Only) (Discrete)

All unadjusted and adjusted Model 1 through 4 analyses of proinsulin in its discrete form for diabetic participants were nonsignificant (Table 18-31(a-h): p>0.07 for each analysis).

Table 18-31. Analysis of Proinsulin (Diabetics Only) (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*139*	*73 (52.5)*	*1.24 (0.81,1.90)*	*0.313*
	Comparison	*221*	*104 (47.1)*		
Officer	Ranch Hand	50	25 (50.0)	1.71 (0.83,3.54)	0.145
	Comparison	76	28 (36.8)		
Enlisted Flyer	Ranch Hand	28	12 (42.9)	0.62 (0.24,1.62)	0.330
	Comparison	42	23 (54.8)		
Enlisted Groundcrew	Ranch Hand	61	36 (59.0)	1.36 (0.72,2.58)	0.348
	Comparison	103	53 (51.5)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*351*	*1.27 (0.79,2.06)*	*0.323*
Officer	125	1.69 (0.76,3.78)	0.199
Enlisted Flyer	65	0.44 (0.14,1.37)	0.155
Enlisted Groundcrew	161	1.57 (0.77,3.22)	0.219

(c) MODEL 2: RANCH HANDS − INITIAL DIOXIN − UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	29	17 (58.6)	0.86 (0.64,1.14)	0.288
Medium	34	22 (64.7)		
High	34	17 (50.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 18-31. Analysis of Proinsulin (Diabetics Only) (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
94	0.70 (0.46,1.05)	0.075

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	221	104 (47.1)		
Background RH	42	17 (40.5)	0.94 (0.47,1.89)	0.873
Low RH	46	27 (58.7)	1.37 (0.70,2.69)	0.353
High RH	51	29 (56.9)	1.45 (0.76,2.76)	0.257
Low plus High RH	97	56 (57.7)	1.41 (0.86,2.34)	0.176

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	215		
Background RH	42	1.24 (0.59,2.62)	0.573
Low RH	45	1.59 (0.75,3.34)	0.225
High RH	49	1.08 (0.53,2.19)	0.831
Low plus High RH	94	1.30 (0.75,2.25)	0.351

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-31. Analysis of Proinsulin (Diabetics Only) (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	25	9 (36.0)	1.08 (0.88,1.32)	0.474
Medium	50	28 (56.0)		
High	64	36 (56.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
136	0.92 (0.71,1.19)	0.536

[a]Relative risk for a twofold increase in 1987 dioxin.

18.2.2.3.21   GADA (Diabetics Only)

In the analysis of GADA for diabetic participants, all unadjusted and adjusted Model 1 through 4 results were nonsignificant (Table 18-32(a-h): p>0.14 for each analysis).

Table 18-32. Analysis of GADA (Diabetics Only)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*139*	*3 (2.2)*	*0.52 (0.14,1.95)*	*0.310*
	Comparison	*221*	*9 (4.1)*		
Officer	Ranch Hand	50	2 (4.0)	1.01 (0.16,6.29)	0.988
	Comparison	76	3 (3.9)		
Enlisted Flyer	Ranch Hand	28	0 (0.0)	--	0.660[a]
	Comparison	42	2 (4.8)		
Enlisted Groundcrew	Ranch Hand	61	1 (1.6)	0.41 (0.05,3.78)	0.433
	Comparison	103	4 (3.9)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of diabetics with GADA present.

--: Results were not presented because of the sparse number of diabetics with GADA present.

Table 18-32. Analysis of GADA (Diabetics Only) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*351*	*0.53 (0.14,1.98)*	*0.321*
Officer	125	1.05 (0.17,6.57)	0.961
Enlisted Flyer	65	--	--
Enlisted Groundcrew	161	0.41 (0.04,3.81)	0.434

--: Results were not presented because of the sparse number of diabetics with GADA present.

Note: Results were not adjusted for race because of the sparse number of diabetic participants with GADA present.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	29	1 (3.4)	1.23 (0.58,2.59)	0.602
Medium	34	1 (2.9)		
High	34	1 (2.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
94	1.11 (0.35,3.53)	0.859

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of diabetic Ranch Hands with GADA present.

Table 18-32. Analysis of GADA (Diabetics Only) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	221	9 (4.1)		
Background RH	42	0 (0.0)	--	0.386[c]
Low RH	46	2 (4.3)	1.15 (0.24,5.58)	0.859
High RH	51	1 (2.0)	0.48 (0.06,3.86)	0.488
Low plus High RH	97	3 (3.1)	0.73 (0.18,2.97)	0.655

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of diabetics with GADA present.

--: Results were not presented because of the sparse number of diabetics with GADA present.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	215		
Background RH	42	--	--
Low RH	45	1.24 (0.24,6.38)	0.794
High RH	49	0.52 (0.06,4.47)	0.555
Low plus High RH	94	0.79 (0.19,3.28)	0.749

[a]Relative risk and confidence interval relative to Comparisons.

--: Results were not presented because of the sparse number of participants with GADA present.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

　　　Results were not adjusted for race because of the sparse number of diabetic participants with GADA present.

Table 18-32. Analysis of GADA (Diabetics Only) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Present**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	25	0 (0.0)	1.62 (0.86,3.07)	0.142
Medium	50	1 (2.0)		
High	64	2 (3.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
136	1.65 (0.78,3.49)	0.162

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of diabetic Ranch Hands with GADA present.

18.2.2.3.22 *Total Testosterone (Continuous)*

All unadjusted and adjusted analyses of total testosterone in its continuous form were nonsignificant for Models 1, 3, and 4 (Table 18-33(a,b,e-h): p>0.07 for each analysis).

The unadjusted Model 2 analysis revealed a significant positive association between initial dioxin and total testosterone in its continuous form (Table 18-33(c): Slope=0.367, p=0.025). After adjusting for covariates, the results were no longer significant (Table 18-33(d): p=0.086).

Table 18-33. Analysis of Total Testosterone (ng/dL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*770*	*409.6*	*1.6*	*0.860*
	Comparison	*1,161*	*408.0*		
Officer	Ranch Hand	303	395.5	-4.0	0.776
	Comparison	457	399.5		
Enlisted Flyer	Ranch Hand	132	424.3	14.8	0.508
	Comparison	182	409.6		
Enlisted Groundcrew	Ranch Hand	335	416.7	1.8	0.898
	Comparison	522	414.9		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*769*	*416.8*	*2.2*	*0.795*
	Comparison	*1,161*	*414.6*		
Officer	Ranch Hand	302	405.7	-0.8	0.954
	Comparison	457	406.4		
Enlisted Flyer	Ranch Hand	132	433.5	11.8	0.569
	Comparison	182	421.6		
Enlisted Groundcrew	Ranch Hand	335	414.6	1.2	0.923
	Comparison	522	413.4		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for $\log_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	139	409.2	405.1	0.109	0.367 (0.163)	0.025*
Medium	143	355.9	353.8			
High	138	427.6	434.2			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of total testosterone versus $\log_2$ (initial dioxin).

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	428.1	0.226	0.308 (0.179)	0.086
Medium	143	371.1			
High	138	439.2			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of total testosterone versus $\log_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,161	408.0	408.9		
Background RH	349	424.2	406.7	-2.2	0.839
Low RH	210	389.8	396.2	-12.7	0.350
High RH	210	403.2	420.4	11.5	0.411
Low plus High RH	420	396.5	408.2	-0.7	0.942

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,161	414.2		
Background RH	348	416.3	2.1	0.852
Low RH	210	415.6	1.4	0.922
High RH	210	417.1	2.9	0.840
Low plus High RH	420	416.3	2.1	0.842

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	257	434.0	0.004	-0.190 (0.107)	0.077
Medium	257	403.1			
High	255	390.1			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of total testosterone versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	256	417.0	0.176	0.009 (0.115)	0.939
Medium	257	416.4			
High	255	392.7			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of total testosterone versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

18.2.2.3.23 Total Testosterone (Discrete)

No significant associations were revealed in the unadjusted and adjusted Model 1 through 4 analyses of total testosterone in its discrete form (Table 18-34(a-h): p>0.13 for each analysis).

Table 18-34. Analysis of Total Testosterone (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*128 (16.6)*	*1.20 (0.94,1.55)*	*0.150*
	Comparison	*1,161*	*165 (14.2)*		
Officer	Ranch Hand	303	54 (17.8)	1.36 (0.91,2.02)	0.132
	Comparison	457	63 (13.8)		
Enlisted Flyer	Ranch Hand	132	21 (15.9)	1.19 (0.63,2.23)	0.591
	Comparison	182	25 (13.7)		
Enlisted Groundcrew	Ranch Hand	335	53 (15.8)	1.09 (0.74,1.59)	0.670
	Comparison	522	77 (14.8)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*1.18 (0.91,1.54)*	*0.207*
Officer	759	1.31 (0.87,1.98)	0.200
Enlisted Flyer	314	1.17 (0.61,2.24)	0.643
Enlisted Groundcrew	857	1.08 (0.73,1.61)	0.688

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	21 (15.1)	0.98 (0.81,1.18)	0.835
Medium	143	32 (22.4)		
High	138	23 (16.7)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 18-34. Analysis of Total Testosterone (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
420	0.95 (0.76,1.19)	0.650

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,161	165 (14.2)		
Background RH	349	52 (14.9)	1.25 (0.89,1.77)	0.200
Low RH	210	35 (16.7)	1.14 (0.76,1.72)	0.527
High RH	210	41 (19.5)	1.29 (0.87,1.90)	0.207
Low plus High RH	420	76 (18.1)	1.21 (0.89,1.65)	0.221

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,161		
Background RH	348	1.22 (0.85,1.75)	0.279
Low RH	210	0.97 (0.63,1.47)	0.875
High RH	210	1.37 (0.91,2.07)	0.135
Low plus High RH	420	1.15 (0.84,1.58)	0.387

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-34. Analysis of Total Testosterone (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	39 (15.2)	1.09 (0.97,1.22)	0.157
Medium	257	39 (15.2)		
High	255	50 (19.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	1.02 (0.88,1.19)	0.800

[a]Relative risk for a twofold increase in 1987 dioxin.

18.2.2.3.24 *Free Testosterone (Continuous)*

All unadjusted and adjusted Model 1 through 4 analyses of free testosterone in its continuous form were nonsignificant (Table 18-35(a-h): p>0.05 for each analysis).

Table 18-35. Analysis of Free Testosterone (pg/mL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*770*	*10.42*	*-0.03*	*0.853*
	Comparison	*1,161*	*10.46*		
Officer	Ranch Hand	303	9.67	-0.42	0.133
	Comparison	457	10.08		
Enlisted Flyer	Ranch Hand	132	10.52	0.45	0.306
	Comparison	182	10.07		
Enlisted Groundcrew	Ranch Hand	335	11.09	0.17	0.549
	Comparison	522	10.92		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Table 18-35. Analysis of Free Testosterone (pg/mL) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*769*	*10.47*	*-0.01*	*0.944*
	Comparison	*1,161*	*10.48*		
Officer	Ranch Hand	302	10.14	-0.33	0.204
	Comparison	457	10.47		
Enlisted Flyer	Ranch Hand	132	10.85	0.47	0.252
	Comparison	182	10.39		
Enlisted Groundcrew	Ranch Hand	335	10.57	0.10	0.695
	Comparison	522	10.47		

[a]Transformed from square root scale.

[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.

[c]P-value was based on difference of means on square root scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	139	10.29	10.22	0.089	0.038 (0.020)	0.061
Medium	143	10.14	10.10			
High	138	10.98	11.10			

[a]Transformed from square root scale.

[b]Adjusted for body mass index at the time of the blood measurement of dioxin.

[c]Slope and standard error based on square root of free testosterone versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	10.70	0.196	-0.003 (0.023)	0.906
Medium	143	10.16			
High	138	10.72			

[a]Transformed from square root scale.

[b]Slope and standard error based on square root of free testosterone versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 18-35. Analysis of Free Testosterone (pg/mL) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,161	10.46	10.47		
Background RH	349	10.36	10.04	-0.43	0.055
Low RH	210	10.29	10.41	-0.06	0.818
High RH	210	10.63	10.95	0.48	0.090
Low plus High RH	420	10.46	10.68	0.21	0.334

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,161	10.47		
Background RH	348	10.26	-0.21	0.332
Low RH	210	10.75	0.28	0.306
High RH	210	10.44	-0.03	0.910
Low plus High RH	420	10.59	0.12	0.554

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-35. Analysis of Free Testosterone (pg/mL) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean**[a]	**R^2**	**Slope (Standard Error)**[b]	**p-Value**
Low	257	10.58	<0.001	-0.001 (0.013)	0.930
Medium	257	10.15			
High	255	10.51			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of free testosterone versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean**[a]	**R^2**	**Adjusted Slope (Standard Error)**[b]	**p-Value**
Low	256	10.79	0.179	-0.011 (0.014)	0.460
Medium	257	10.75			
High	255	10.33			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of free testosterone versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

18.2.2.3.25   Free Testosterone (Discrete)

No significant overall group difference was seen in the unadjusted and adjusted Model 1 analyses of categorized free testosterone (Table 18-36(a,b): p>0.43 for each analysis). After stratifying by military occupation, however, a significant difference between Ranch Hands and Comparisons was seen among officers in both the unadjusted and adjusted analyses (Table 18-36(a,b): Unadjusted RR=1.92, p=0.025; Adjusted RR=1.87, p=0.039). Among officers, Ranch Hands had a higher percentage of abnormally low free testosterone values (9.2%) versus Comparisons (5.0%).

No significant relations were seen in the unadjusted and adjusted Model 2 through 4 analyses of free testosterone in its discrete form (Table 18-36(c-h): p>0.09 for each analysis).

Table 18-36. Analysis of Free Testosterone (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*49 (6.4)*	*1.16 (0.79,1.71)*	*0.437*
	Comparison	*1,161*	*64 (5.5)*		
Officer	Ranch Hand	303	28 (9.2)	1.92 (1.08,3.40)	0.025*
	Comparison	457	23 (5.0)		
Enlisted Flyer	Ranch Hand	132	9 (6.8)	0.71 (0.31,1.65)	0.425
	Comparison	182	17 (9.3)		
Enlisted Groundcrew	Ranch Hand	335	12 (3.6)	0.77 (0.38,1.56)	0.471
	Comparison	522	24 (4.6)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*1.10 (0.74,1.64)*	*0.633*
Officer	759	1.87 (1.03,3.39)	0.039*
Enlisted Flyer	314	0.65 (0.27,1.54)	0.326
Enlisted Groundcrew	857	0.75 (0.36,1.55)	0.439

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	10 (7.2)	0.94 (0.70,1.27)	0.686
Medium	143	10 (7.0)		
High	138	7 (5.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 18-36. Analysis of Free Testosterone (Discrete) (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
420	1.14 (0.81,1.61)	0.459

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Low	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,161	64 (5.5)		
Background RH	349	22 (6.3)	1.41 (0.85,2.36)	0.184
Low RH	210	14 (6.7)	1.11 (0.60,2.06)	0.733
High RH	210	13 (6.2)	0.94 (0.50,1.76)	0.836
Low plus High RH	420	27 (6.4)	1.02 (0.63,1.65)	0.934

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,161		
Background RH	348	1.24 (0.73,2.11)	0.432
Low RH	210	0.91 (0.49,1.69)	0.758
High RH	210	1.19 (0.61,2.31)	0.617
Low plus High RH	420	1.04 (0.63,1.70)	0.887

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-36. Analysis of Free Testosterone (Discrete) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Low**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	257	13 (5.1)	1.08 (0.90,1.29)	0.421
Medium	257	20 (7.8)		
High	255	16 (6.3)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
768	1.25 (0.96,1.62)	0.093

[a]Relative risk for a twofold increase in 1987 dioxin.

18.2.2.3.26 Estradiol (Measurements Above Sensitivity Limit) (Continuous)

All unadjusted and adjusted Model 1 through 4 analyses of estradiol values measured above the instrument sensitivity limit of 10 pg/mL were nonsignificant (Table 18-37(a-h): p≥0.32 for each analysis).

Table 18-37. Analysis of Estradiol (pg/mL) (Measurements Above Sensitivity Limit) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*503*	*22.06*	*0.41*	*0.526*
	Comparison	*746*	*21.65*		
Officer	Ranch Hand	192	22.09	0.50	0.629
	Comparison	294	21.58		
Enlisted Flyer	Ranch Hand	91	22.14	-0.15	0.927
	Comparison	117	22.28		
Enlisted Groundcrew	Ranch Hand	220	22.01	0.52	0.595
	Comparison	335	21.49		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*503*	*23.69*	*0.39*	*0.580*
	Comparison	*746*	*23.30*		
Officer	Ranch Hand	192	23.75	0.50	0.657
	Comparison	294	23.25		
Enlisted Flyer	Ranch Hand	91	23.59	-0.27	0.873
	Comparison	117	23.86		
Enlisted Groundcrew	Ranch Hand	220	23.53	0.53	0.606
	Comparison	335	22.99		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	98	22.80	22.84	0.001	-0.005 (0.023)	0.844
Medium	89	20.65	20.66			
High	94	21.64	21.60			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of estradiol versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	98	24.28	0.016	-0.001 (0.028)	0.977
Medium	89	21.98			
High	94	22.78			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of estradiol versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	746	21.65	21.65		
Background RH	221	22.44	22.52	0.87	0.320
Low RH	139	21.91	21.89	0.24	0.814
High RH	142	21.52	21.45	-0.20	0.846
Low plus High RH	281	21.71	21.67	0.02	0.980

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	746	23.28		
Background RH	221	24.13	0.85	0.370
Low RH	139	23.24	-0.04	0.968
High RH	142	23.28	0.00	0.999
Low plus High RH	281	23.26	-0.02	0.980

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	168	21.59	<0.001	0.001 (0.014)	0.930
Medium	167	23.25			
High	167	21.30			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of estradiol versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	168	23.04	0.009	0.006 (0.017)	0.708
Medium	167	24.67			
High	167	22.72			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of estradiol versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

18.2.2.3.27 *Estradiol (Discrete)*

No significant associations were seen in the unadjusted and adjusted Model 1 through 4 analyses of estradiol in its discrete form (Table 18-38(a-h): p>0.07 for each analysis).

Table 18-38. Analysis of Estradiol (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*23 (3.0)*	*1.16 (0.67,2.01)*	*0.597*
	Comparison	*1,161*	*30 (2.6)*		
Officer	Ranch Hand	303	11 (3.6)	1.68 (0.71,4.02)	0.240
	Comparison	457	10 (2.2)		
Enlisted Flyer	Ranch Hand	132	2 (1.5)	0.33 (0.07,1.60)	0.171
	Comparison	182	8 (4.4)		
Enlisted Groundcrew	Ranch Hand	335	10 (3.0)	1.31 (0.56,3.06)	0.537
	Comparison	522	12 (2.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*1.16 (0.67,2.01)*	*0.608*
Officer	759	1.67 (0.70,3.99)	0.247
Enlisted Flyer	314	0.33 (0.07,1.59)	0.166
Enlisted Groundcrew	857	1.32 (0.56,3.10)	0.522

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	1 (0.7)	1.52 (0.97,2.37)	0.073
Medium	143	3 (2.1)		
High	138	5 (3.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
420	1.54 (0.97,2.45)	0.077

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and military occupation because of the sparse number of Ranch Hands with high estradiol.

Table 18-38. Analysis of Estradiol (Discrete) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,161	30 (2.6)		
Background RH	349	14 (4.0)	1.67 (0.87,3.21)	0.123
Low RH	210	3 (1.4)	0.53 (0.16,1.77)	0.305
High RH	210	6 (2.9)	1.05 (0.43,2.57)	0.912
Low plus High RH	420	9 (2.1)	0.75 (0.34,1.65)	0.475

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,161		
Background RH	348	1.70 (0.87,3.32)	0.119
Low RH	210	0.48 (0.14,1.60)	0.231
High RH	210	1.08 (0.43,2.71)	0.872
Low plus High RH	420	0.72 (0.32,1.60)	0.419

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	8 (3.1)	0.98 (0.76,1.28)	0.905
Medium	257	8 (3.1)		
High	255	7 (2.7)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 18-38. Analysis of Estradiol (Discrete) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
768	0.97 (0.71,1.33)	0.847

[a]Relative risk for a twofold increase in 1987 dioxin.

18.2.2.3.28 *LH (Continuous)*

The unadjusted and adjusted Model 1 analyses of LH in its continuous form showed no group differences among all participants (Table 18-39(a,b): p>0.11 for each analysis). After stratifying by military occupation, however, a significant difference between Ranch Hands and Comparisons was seen among officers in both the unadjusted and adjusted analyses (Table 18-39(a,b): difference of means=0.46 mIU/mL, p=0.034; difference of adjusted means=0.40 mIU/mL, p=0.040). Ranch Hand officers had a higher adjusted mean LH value (4.49 mIU/mL) than Comparison officers (4.09 mIU/mL).

A significant inverse association was revealed between initial dioxin and LH in the unadjusted Model 2 analysis (Table 18-39(c): Slope=-0.051, p=0.020). After covariate adjustment, the results were no longer significant (Table 18-39(d): p=0.217).

Both the unadjusted and adjusted Model 3 analyses revealed a significant difference in mean LH levels between Ranch Hands in the low dioxin category and Comparisons (Table 18-39(e,f): difference of means=0.61 mIU/mL, p=0.006, for unadjusted analysis; difference of adjusted means=0.51 mIU/mL, p=0.015, for adjusted analysis). Ranch Hands in the low dioxin category had an adjusted mean LH value of 4.81 mIU/mL versus 4.30 mIU/mL for Comparisons.

The unadjusted and adjusted Model 4 analyses showed no significant associations between 1987 dioxin and LH in its continuous form (Table 18-39(g,h): p>0.05 for each analysis).

Table 18-39. Analysis of LH (mIU/mL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*770*	*4.56*	*0.20*	*0.125*
	Comparison	*1,161*	*4.36*		
Officer	Ranch Hand	303	4.83	0.46	0.034*
	Comparison	457	4.37		
Enlisted Flyer	Ranch Hand	132	4.49	-0.03	0.925
	Comparison	182	4.52		
Enlisted Groundcrew	Ranch Hand	335	4.35	0.06	0.741
	Comparison	522	4.29		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*769*	*4.52*	*0.20*	*0.118*
	Comparison	*1,161*	*4.33*		
Officer	Ranch Hand	302	4.49	0.40	0.040*
	Comparison	457	4.09		
Enlisted Flyer	Ranch Hand	132	4.28	-0.08	0.787
	Comparison	182	4.36		
Enlisted Groundcrew	Ranch Hand	335	4.73	0.12	0.560
	Comparison	522	4.61		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Table 18-39. Analysis of LH (mIU/mL) (Continuous) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	139	5.10	5.12	0.025	-0.051 (0.022)	0.020*
Medium	143	4.10	4.11			
High	138	4.46	4.43			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of LH versus log$_2$ (initial dioxin).

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	5.04	0.052	-0.031 (0.025)	0.217
Medium	143	4.23			
High	138	4.66			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of LH versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 18-39. Analysis of LH (mIU/mL) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,161	4.36	4.35		
Background RH	349	4.59	4.60	0.25	0.156
Low RH	210	4.97	4.96	0.61	0.006**
High RH	210	4.13	4.12	-0.23	0.235
Low plus High RH	420	4.53	4.52	0.17	0.307

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,161	4.30		
Background RH	348	4.51	0.21	0.208
Low RH	210	4.81	0.51	0.015*
High RH	210	4.20	-0.10	0.614
Low plus High RH	420	4.49	0.19	0.213

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-39. Analysis of LH (mIU/mL) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	257	4.79	0.005	-0.026 (0.014)	0.057
Medium	257	4.73			
High	255	4.17			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of LH versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	256	4.85	0.049	-0.016 (0.016)	0.321
Medium	257	4.68			
High	255	4.34			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of LH versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

18.2.2.3.29 LH (Discrete)

All unadjusted and adjusted Model 1 through 4 analyses of LH in its discrete form were nonsignificant (Table 18-40(a-h): p>0.12 for each analysis).

Table 18-40. Analysis of LH (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*35 (4.5)*	*0.75 (0.50,1.14)*	*0.179*
	Comparison	*1,161*	*69 (5.9)*		
Officer	Ranch Hand	303	14 (4.6)	0.71 (0.37,1.38)	0.315
	Comparison	457	29 (6.3)		
Enlisted Flyer	Ranch Hand	132	6 (4.5)	0.67 (0.25,1.85)	0.443
	Comparison	182	12 (6.6)		
Enlisted Groundcrew	Ranch Hand	335	15 (4.5)	0.83 (0.43,1.57)	0.562
	Comparison	522	28 (5.4)		

Table 18-40. Analysis of LH (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*0.74 (0.48,1.13)*	*0.155*
Officer	759	0.71 (0.37,1.39)	0.318
Enlisted Flyer	314	0.61 (0.22,1.68)	0.336
Enlisted Groundcrew	857	0.83 (0.43,1.61)	0.582

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	5 (3.6)	0.95 (0.66,1.37)	0.789
Medium	143	6 (4.2)		
High	138	6 (4.3)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
420	0.99 (0.66,1.51)	0.980

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,161	69 (5.9)		
Background RH	349	18 (5.2)	0.89 (0.52,1.53)	0.677
Low RH	210	9 (4.3)	0.70 (0.34,1.43)	0.325
High RH	210	8 (3.8)	0.61 (0.29,1.28)	0.191
Low plus High RH	420	17 (4.0)	0.65 (0.38,1.12)	0.124

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-40. Analysis of LH (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,161		
Background RH	348	0.84 (0.48,1.48)	0.553
Low RH	210	0.64 (0.31,1.32)	0.227
High RH	210	0.67 (0.31,1.48)	0.323
Low plus High RH	420	0.66 (0.37,1.15)	0.142

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	15 (5.8)	0.92 (0.74,1.15)	0.477
Medium	257	10 (3.9)		
High	255	10 (3.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log_2 (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	0.92 (0.70,1.20)	0.524

[a]Relative risk for a twofold increase in 1987 dioxin.

18.2.2.3.30   FSH (Continuous)

The unadjusted Model 1 analysis of FSH in its continuous form showed no significant group differences (Table 18-41(a): p=0.562). After stratifying by occupation, a significant difference between Ranch Hands and Comparisons was seen among officers (Table 18-41(a): difference of means=0.63 mIU/mL, p=0.043). In the adjusted Model 1 analyses of FSH, however, no significant group differences were noted among all participants or within each military occupation (Table 18-41(b): p>0.05 for each analysis).

A significant inverse association between initial dioxin and FSH in its continuous form was seen in the unadjusted Model 2 analysis (Table 18-41(c): Slope=-0.061, p=0.011). After covariate adjustment, the results were no longer significant (Table 18-41(d): p=0.267).

The unadjusted Model 3 analysis revealed a significant difference in mean FSH levels between Ranch Hands in the low dioxin category and Comparisons (Table 18-41(e): difference of means=0.72 mIU/mL, p=0.019). After adjusting for covariates, the results were nonsignificant (Table 18-41(f): p>0.06 for each contrast).

No significant associations between 1987 dioxin and FSH in its continuous form were revealed in the unadjusted and adjusted Model 4 analyses (Table 18-41(g,h): p>0.30 for each analysis).

Table 18-41. Analysis of FSH (mIU/mL) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED					
Occupational Category	**Group**	**n**	**Unadjusted Mean[a]**	**Difference of Unadjusted Means[b]**	**p-Value[c]**
All	*Ranch Hand*	*770*	*5.78*	*0.11*	*0.562*
	Comparison	*1,161*	*5.68*		
Officer	Ranch Hand	303	6.44	0.63	0.043*
	Comparison	457	5.82		
Enlisted Flyer	Ranch Hand	132	5.56	-0.23	0.607
	Comparison	182	5.79		
Enlisted Groundcrew	Ranch Hand	335	5.32	-0.19	0.452
	Comparison	522	5.52		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Table 18-41. Analysis of FSH (mIU/mL) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*769*	*5.64*	*0.10*	*0.557*
	Comparison	*1,161*	*5.54*		
Officer	Ranch Hand	302	5.80	0.52	0.053
	Comparison	457	5.28		
Enlisted Flyer	Ranch Hand	132	5.17	-0.29	0.466
	Comparison	182	5.46		
Enlisted Groundcrew	Ranch Hand	335	5.85	-0.13	0.621
	Comparison	522	5.98		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	139	6.68	6.72	0.035	-0.061 (0.024)	0.011*
Medium	143	5.18	5.19			
High	138	5.54	5.49			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of FSH versus log_2 (initial dioxin).

*: Statistically significant ($0.010 <$ p-value ≤ 0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	139	6.16	0.072	-0.030 (0.027)	0.267
Medium	143	5.05			
High	138	5.53			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of FSH versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 18-41. Analysis of FSH (mIU/mL) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,161	5.68	5.68		
Background RH	349	5.81	5.85	0.17	0.474
Low RH	210	6.41	6.40	0.72	0.019*
High RH	210	5.17	5.15	-0.53	0.056
Low plus High RH	420	5.76	5.74	0.06	0.774

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,161	5.51		
Background RH	348	5.57	0.06	0.791
Low RH	210	6.05	0.54	0.061
High RH	210	5.29	-0.22	0.431
Low plus High RH	420	5.66	0.15	0.488

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-41. Analysis of FSH (mIU/mL) (Continuous) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	257	5.93	0.001	-0.015 (0.015)	0.309
Medium	257	6.29			
High	255	5.19			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of FSH versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	256	5.83	0.076	0.011 (0.017)	0.523
Medium	257	6.05			
High	255	5.50			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of FSH versus log_2 (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

18.2.2.3.31 FSH (Discrete)

No significant associations with FSH in its discrete form were revealed in the unadjusted and adjusted Model 1 through 4 analyses (Table 18-42(a-h): p>0.10 for each analysis).

Table 18-42. Analysis of FSH (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*770*	*44 (5.7)*	*0.94 (0.64,1.39)*	*0.773*
	Comparison	*1,161*	*70 (6.0)*		
Officer	Ranch Hand	303	26 (8.6)	1.21 (0.71,2.06)	0.493
	Comparison	457	33 (7.2)		
Enlisted Flyer	Ranch Hand	132	9 (6.8)	0.81 (0.35,1.92)	0.640
	Comparison	182	15 (8.2)		
Enlisted Groundcrew	Ranch Hand	335	9 (2.7)	0.63 (0.29,1.38)	0.246
	Comparison	522	22 (4.2)		

Table 18-42. Analysis of FSH (Discrete) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,930*	*0.92 (0.62,1.37)*	*0.692*
Officer	759	1.22 (0.70,2.11)	0.481
Enlisted Flyer	314	0.75 (0.31,1.80)	0.523
Enlisted Groundcrew	857	0.63 (0.28,1.40)	0.255

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	139	8 (5.8)	0.79 (0.56,1.12)	0.174
Medium	143	9 (6.3)		
High	138	5 (3.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
420	0.92 (0.61,1.39)	0.699

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,161	70 (6.0)		
Background RH	349	22 (6.3)	1.08 (0.66,1.78)	0.758
Low RH	210	15 (7.1)	1.19 (0.67,2.12)	0.562
High RH	210	7 (3.3)	0.52 (0.24,1.16)	0.109
Low plus High RH	420	22 (5.2)	0.79 (0.47,1.33)	0.368

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 18-42. Analysis of FSH (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,161		
Background RH	348	0.95 (0.56,1.59)	0.835
Low RH	210	1.03 (0.57,1.86)	0.933
High RH	210	0.73 (0.32,1.66)	0.449
Low plus High RH	420	0.86 (0.50,1.48)	0.592

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) High	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	16 (6.2)	0.92 (0.76,1.12)	0.407
Medium	257	18 (7.0)		
High	255	10 (3.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
768	1.05 (0.80,1.38)	0.700

[a]Relative risk for a twofold increase in 1987 dioxin.

18.3 DISCUSSION

As part of the endocrinology assessment, Ranch Hands and Comparisons were evaluated for thyroid disease, diabetes, and testosterone and other sex hormone levels. Particular attention was given to the possible effects that herbicides and dioxin could have had on the pituitary, gonadal, and thyroid glands, as well as the possible relation between herbicide exposure or dioxin levels and diabetes and insulin resistance.

Using standard diabetes definitions employed in this study (82) and based on estimates from the CDC, the prevalence of diabetes mellitus in U.S. adults aged 45 to 64 increased from approximately 6 percent to 9 percent between 1997 and 2002 (83). The most likely factor driving this increase is the steadily rising prevalence of obesity. According to the CDC, the percentage of overweight Americans rose from 51 percent to 64 percent during the same time span (83). Because both gonadal functions and diabetes are strikingly affected by obesity, as well as aging, it is important to correct for possible effects of increasing body weight and aging when trying to isolate the potential effects herbicides and dioxin has on the human body.

A review of the dependent variable-covariate associations showed findings that were consistent with existing literature on Type 2 diabetes. Mokdad and colleagues conducted a study in 2001 and concluded that there was a correlation of increasing diabetes risk and severity with increasing age, adiposity, a family history of diabetes, and non-Caucasian race (83). Likewise, the significant decline in total testosterone with increasing age is consistent with the current literature. A decline in total testosterone is usually not accompanied by an increase in LH, and no association was present between total testosterone and LH in these data. No unusual patterns were seen as compared to age-matched populations already studied (84).

For a statistically significant finding to be physiologically or clinically significant, the finding should be consistent with physiology, have some consistency with known data regarding clinically significant findings and, ideally, be reproducible in more than one statistical model. Only the diabetes data seem to fulfill each of these criteria. The known associations of Type 2 diabetes with obesity and insulin resistance fit the model analysis and were consistent across two or more model assessments, with a dose-response effect evident regarding prevalence and severity of diabetes. For the thyroid and gonadal findings, generally only one model was significant and no positive dose-response relation was seen. These considerations and the small differences in means in the thyroid and gonadal measures make a clinically significant finding very unlikely.

As indicated in the 1997 follow-up examination and again in the 2002 examination, significant associations exist between dioxin levels and diabetes. A greater prevalence of diabetes, diabetes of greater severity (as evidenced by the need for more medication and higher hemoglobin A1c levels), and a shorter time to onset of diabetes were seen more often in Ranch Hands as 1987 dioxin levels increased. The association between 1987 dioxin and diabetes was similar regardless of whether the participant was obese. The mechanism for the increase in diabetes is not clear. In animals exposed to 100 mg/kg of dioxin, a reduction in insulin levels relative to glucose was seen (25), suggesting a possible direct pancreatic effect. In the 2002 follow-up examination, however, a statistically higher fasting insulin level that was more consistent with increased insulin resistance was seen in Ranch Hand participants. Insulin resistance is a near universal finding in Type 2 diabetes mellitus, but it is also found in about 25 percent of the U.S. population and about 45 percent in subjects aged 60 and higher based on clinical criteria (85). No difference was seen in the prevalence of GADA, a marker of Type 1 diabetes. These results are most compatible with an "unmasking" or acceleration of Type 2 diabetes, possibly by worsening insulin resistance. This could be explained by a direct effect of dioxin or by a slightly accelerating rate of weight gain in this group of individuals. Some effect on insulin release cannot be excluded based on these data.

As for a dioxin effect related to thyroid disease, the 2002 examination data did not support such a relation. No differences of the thyroid or in anti-thyroid antibodies were observed during the 2002 physical examination. Although statistically significant, the difference in adjusted mean TSH (mean of 1.653 μIU/mL in Ranch Hands versus 1.557 μIU/mL in Comparisons) was not considered clinically significant. The same was true for the free T_4 values in enlisted flyers (mean of 1.115 ng/dL in Ranch Hands versus 1.054 ng/dL in Comparisons). If a primary thyroid effect were present, one would expect the TSH to

move in the opposite direction of the free T_4, which was not seen in these data. There may be, however, other mechanisms of action.

A similar conclusion may be drawn regarding reproductive hormones. SHBG is known to rise with increasing age and adiposity. In the Massachusetts Male Aging Study of healthy men aged 40 to 70, total testosterone was seen to fall at a rate of 0.8 percent per year and free testosterone at 2 percent per year (84). The difference in adjusted free testosterone means in Ranch Hands versus Comparisons was 10.95 versus 10.47, respectively. The LH means for Ranch Hand and Comparison officers were 4.49 mIU/mL versus 4.09 mIU/mL, respectively. Both were well within one standard deviation of normal-age matched populations. No evidence of a dose-response effect was seen based on categorized dioxin or 1987 dioxin levels.

In summary, the association noted at previous AFHS examinations between Type 2 diabetes mellitus and dioxin persisted. A higher prevalence of diabetes, as well as severity, as dioxin increased was evident, even after adjustment for such factors as age and body mass index. In contrast, the association of dioxin with thyroid or gonadal abnormalities appeared weak at best and unlikely to be clinically significant.

18.4   SUMMARY

The endocrinology assessment was based on questionnaire, physical examination, and laboratory data. Associations with herbicide exposure (i.e., group − Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable in the endocrinology assessment. The significant adjusted results are discussed in the sections below.

18.4.1   Model 1: Group Analysis

Ranch Hands had a significantly higher mean TSH value than Comparisons when examined across all participants and within officers. A significant difference between Ranch Hands and Comparisons was seen among officers in the analysis of LH in its continuous form, as well as in the analyses of 2-hour postprandial urinary glucose and free testosterone in their discrete form. In each case, Ranch Hand officers had a higher mean value or percent abnormal than Comparison officers.

Comparison enlisted flyers had a lower mean free T_4 value and a greater percentage of abnormally low values than Ranch Hand enlisted flyers. When diabetes was classified using the pre-2002 AFHS definition, a significantly higher percentage of Comparison enlisted groundcrew used nothing to treat their diabetes compared to Ranch Hand enlisted groundcrew. Among enlisted groundcrew, Ranch Hands had significantly lower mean 2-hour postprandial glucose and 2-hour postprandial insulin levels than Comparisons. Ranch Hand enlisted groundcrew also had fewer abnormally high 2-hour postprandial insulin values than Comparison enlisted groundcrew.

The results of the group analysis are shown in Table 18-43.

Table 18-43. Summary of Group Analysis (Model 1) for Endocrine Variables (Ranch Hands vs. Comparisons)

	UNADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Medical Records				
Past Thyroid Disease (D)	ns	ns	ns	ns
Composite Diabetes Indicator (2002 AFHS diabetes definition) (D)	ns	ns	ns	ns
Composite Diabetes Indicator (pre-2002 AFHS diabetes definition) (D)	ns	NS	ns	ns
Diabetic Control (2002 AFHS diabetes definition) (D)				
No Treatment vs. Nondiabetic	ns	NS	NS	ns
Diet and Exercise vs. Nondiabetic	ns	ns	NS	ns
Oral Hypoglycemics vs. Nondiabetic	ns	ns	ns	NS
Requiring Insulin vs. Nondiabetic	NS	NS	ns	NS
Diabetic Control (pre-2002 AFHS diabetes definition) (D)				
No Treatment vs. Nondiabetic	ns	NS	ns	p=0.036 (0.51)
Diet and Exercise vs. Nondiabetic	ns	ns	NS	ns
Oral Hypoglycemics vs. Nondiabetic	ns	ns	ns	NS
Requiring Insulin vs. Nondiabetic	NS	NS	ns	NS
Time to Diabetes Onset (2002 AFHS diabetes definition) (C)[a]	ns	ns	ns	ns
Time to Diabetes Onset (pre-2002 AFHS diabetes definition) (C)[a]	ns	NS	ns	ns
Physical Examination				
Thyroid Gland (D)	ns	ns	ns	ns
Testicular Examination (D)	NS	ns	NS	NS
Laboratory				
TSH (C)	p=0.023 (0.108)	p=0.010 (0.211)	ns	NS
TSH (D)				
Low vs. Normal	ns	ns	NS	ns
High vs. Normal	NS	NS	NS	NS
Free T_4 (C)[b]	p=0.047 (0.016)	NS	p=0.001 (0.062)	NS
Free T_4 (D)	ns	NS	p=0.025 (0.37)	ns
Anti-Thyroid Antibodies (D)	ns	ns	NS	ns
Fasting Glucose (C)	ns	NS	ns	ns
Fasting Glucose (D)	NS	NS	ns	NS
2-hour Postprandial Glucose (C)	ns	NS	ns	p=0.013 (-6.7)
2-hour Postprandial Glucose (D)	NS	NS	ns	ns
2-hour Postprandial Urinary Glucose (D)	NS	NS	NS	ns
Fasting Insulin (C)	NS	NS	ns	NS
Fasting Insulin (D)				
Low vs. Normal	ns	NS	ns	ns
High vs. Normal	p=0.046 (1.45)	NS	ns	NS

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
2-hour Postprandial Insulin (C)	ns	NS	ns	ns
2-hour Postprandial Insulin (D)				
Low vs. Normal	NS	NS	ns	NS
High vs. Normal	ns	NS	ns	ns
Hemoglobin A1c (C)	NS	ns	NS	NS
Hemoglobin A1c (D)	ns	ns	ns	NS
C-peptide (C)	NS	NS	ns	ns
C-peptide (D)	NS	NS	ns	ns
Proinsulin (C)	NS	NS	NS	NS
Proinsulin (D)	NS	NS	ns	NS
GADA (D)	ns	NS	ns	ns
Total Testosterone (C)[b]	NS	ns	NS	NS
Total Testosterone (D)	NS	NS	NS	NS
Free Testosterone (C)[b]	ns	ns	NS	NS
Free Testosterone (D)	NS	p=0.025 (1.92)	ns	ns
Estradiol (C)	NS	NS	ns	NS
Estradiol (D)	NS	NS	ns	NS
LH (C)	NS	p=0.034 (0.46)	ns	NS
LH (D)	ns	ns	ns	ns
FSH (C)	NS	p=0.043 (0.63)	ns	ns
FSH (D)	ns	NS	ns	ns

[a]A hazard ratio was used. A hazard ratio greater than 1.0 implied a shorter time to the onset of diabetes for Ranch Hands than for Comparisons. A hazard ratio less than 1.0 implied a longer time to the onset of diabetes for Ranch Hands than for Comparisons.

[b]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse for this variable.

Note: NS or ns: Not significant ($p>0.05$).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

The p-value was given if $p\leq0.05$. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Past Thyroid Disease (D)	ns	ns	ns	ns
Composite Diabetes Indicator (2002 AFHS diabetes definition) (D)	ns	ns	ns	ns
Composite Diabetes Indicator (pre-2002 AFHS diabetes definition) (D)	ns	NS	ns	ns
Diabetic Control (2002 AFHS diabetes definition) (D)				
No Treatment vs. Nondiabetic	ns	NS	NS	ns
Diet and Exercise vs. Nondiabetic	ns	ns	NS	ns
Oral Hypoglycemics vs. Nondiabetic	ns	ns	ns	NS
Requiring Insulin vs. Nondiabetic	NS	NS	ns	NS
Diabetic Control (pre-2002 AFHS diabetes definition) (D)				
No Treatment vs. Nondiabetic	ns	NS	ns	p=0.037 (0.51)
Diet and Exercise vs. Nondiabetic	ns	ns	NS	ns
Oral Hypoglycemics vs. Nondiabetic	ns	ns	ns	NS
Requiring Insulin vs. Nondiabetic	NS	NS	ns	NS
Time to Diabetes Onset (2002 AFHS diabetes definition) (C)[a]	ns	ns	ns	ns
Time to Diabetes Onset (pre-2002 AFHS diabetes definition) (C)[a]	ns	ns	ns	ns
Physical Examination				
Thyroid Gland (D)	ns	ns	--	ns
Testicular Examination (D)	NS	ns	NS	NS
Laboratory				
TSH (C)	p=0.024 (0.096)	p=0.009 (0.189)	ns	NS
TSH (D)				
Low vs. Normal	ns	--	NS	--
High vs. Normal	NS	NS	NS	NS
Free T_4 (C)[b]	NS	NS	p=0.002 (0.061)	NS
Free T_4 (D)	ns	NS	p=0.026 (0.37)	ns
Anti-Thyroid Antibodies (D)	ns	ns	NS	--
Fasting Glucose (C)	ns	ns	NS	NS
Fasting Glucose (D)	NS	NS	ns	NS
2-hour Postprandial Glucose (C)	ns	NS	NS	p=0.006 (-7.4)
2-hour Postprandial Glucose (D)	NS	NS	NS	ns
2-hour Postprandial Urinary Glucose (D)	NS	p=0.050 (1.48)	NS	ns
Fasting Insulin (C)	NS	NS	ns	NS
Fasting Insulin (D)				
Low vs. Normal	ns	NS	ns	ns
High vs. Normal	NS	NS	ns	NS

Variable	ADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
2-hour Postprandial Insulin (C)	ns	NS	NS	p=0.033 (-7.64)
2-hour Postprandial Insulin (D)				
Low vs. Normal	NS	NS	ns	NS
High vs. Normal	ns	NS	NS	p=0.043 (0.70)
Hemoglobin A1c (C)	NS	ns	NS	NS
Hemoglobin A1c (D)	ns	ns	ns	NS
C-peptide (C)	NS	NS	ns	ns
C-peptide (D)	NS	NS	ns	ns
Proinsulin (C)	NS	ns	NS	NS
Proinsulin (D)	NS	NS	ns	NS
GADA (D)	ns	NS	--	ns
Total Testosterone (C)[b]	NS	ns	NS	NS
Total Testosterone (D)	NS	NS	NS	NS
Free Testosterone (C)[b]	ns	ns	NS	NS
Free Testosterone (D)	NS	p=0.039 (1.87)	ns	ns
Estradiol (C)	NS	NS	ns	NS
Estradiol (D)	NS	NS	ns	NS
LH (C)	NS	p=0.040 (0.40)	ns	NS
LH (D)	ns	ns	ns	ns
FSH (C)	NS	NS	ns	ns
FSH (D)	ns	NS	ns	ns

[a]A hazard ratio was used. A hazard ratio greater than 1.0 implies a shorter time to the onset of diabetes for Ranch Hands than for Comparisons. A hazard ratio less than 1.0 implies a longer time to the onset of diabetes for Ranch Hands than for Comparisons.

[b]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse for this variable.

--: Analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
       C: Continuous form of dependent variable.
       D: Discrete form of dependent variable.

      The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

      A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

18.4.2 Model 2: Initial Dioxin Analysis

The adjusted Model 2 analyses revealed a significant positive association between diabetes and initial dioxin when using the pre-2002 AFHS definition. In addition, time to diabetes onset decreased as the initial dioxin level increased when using the pre-2002 AFHS definition. Significant positive relations were seen between initial dioxin and Ranch Hands requiring insulin to control diabetes. A significant positive association was seen between initial dioxin and fasting insulin in both its continuous and discrete form. A significant inverse association was seen between C-peptide in its continuous form and initial dioxin. The results of all unadjusted and adjusted Model 2 analyses are summarized in Table 18-44.

Table 18-44. Summary of Initial Dioxin Analysis (Model 2) for Endocrine Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Past Thyroid Disease (D)	NS	NS
Composite Diabetes Indicator (2002 AFHS diabetes definition) (D)	NS	NS
Composite Diabetes Indicator (pre-2002 AFHS diabetes definition) (D)	NS	p=0.010 (1.34)
Diabetic Control (2002 AFHS diabetes definition) (D)		
No Treatment vs. Nondiabetic	ns	ns
Diet and Exercise vs. Nondiabetic	ns	ns
Oral Hypoglycemics vs. Nondiabetic	NS	NS
Requiring Insulin vs. Nondiabetic	p=0.004 (1.76)	p<0.001 (2.78)
Diabetic Control (pre-2002 AFHS diabetes definition) (D)		
No Treatment vs. Nondiabetic	ns	NS
Diet and Exercise vs. Nondiabetic	ns	ns
Oral Hypoglycemics vs. Nondiabetic	NS	NS
Requiring Insulin vs. Nondiabetic	p=0.003 (1.79)	p<0.001 (2.90)
Time to Diabetes Onset (2002 AFHS diabetes definition) (C)[a]	NS	NS
Time to Diabetes Onset (pre-2002 AFHS diabetes definition) (C)[a]	NS	p=0.033 (1.21)
Physical Examination		
Thyroid Gland (D)	ns	ns
Testicular Examination (D)	NS	NS
Laboratory		
TSH (C)	ns	NS
TSH (D)		
Low vs. Normal	NS	NS
High vs. Normal	ns	NS
Free T_4 (C)[b]	ns	ns
Free T_4 (D)	ns	NS
Anti-Thyroid Antibodies (D)	ns	ns
Fasting Glucose (C)	NS	NS
Fasting Glucose (D)	NS	NS
2-hour Postprandial Glucose (C)	ns	NS
2-hour Postprandial Glucose (D)	p=0.037 (0.79)	ns
2-hour Postprandial Urinary Glucose (D)	NS	NS
Fasting Insulin (C)	p=0.030 (0.047)	p=0.014 (0.056)
Fasting Insulin (D)		
Low vs. Normal	ns	ns
High vs. Normal	p=0.019 (1.31)	p=0.006 (1.54)

Variable	Unadjusted	Adjusted
2-hour Postprandial Insulin (C)	NS	NS
2-hour Postprandial Insulin (D)		
Low vs. Normal	NS	NS
High vs. Normal	NS	NS
Hemoglobin A1c (C)	p=0.014 (0.032)	NS
Hemoglobin A1c (D)	p=0.017 (1.51)	NS
C-peptide (C)	p=0.007 (-0.088)	p=0.017 (-0.091)
C-peptide (D)	ns	ns
Proinsulin (C)	ns	ns
Proinsulin (D)	ns	ns
GADA (D)	NS	NS
Total Testosterone (C)[b]	p=0.025 (0.367)	NS
Total Testosterone (D)	ns	ns
Free Testosterone (C)[b]	NS	ns
Free Testosterone (D)	ns	NS
Estradiol (C)	ns	ns
Estradiol (D)	NS	NS
LH (C)	p=0.020 (-0.051)	ns
LH (D)	ns	ns
FSH (C)	p=0.011 (-0.061)	ns
FSH (D)	ns	ns

[a]A hazard ratio was used. A hazard ratio greater than 1.0 implies that onset of diabetes becomes shorter as initial dioxin increases. A hazard ratio less than 1.0 implies that onset of diabetes becomes longer as initial dioxin increases.

[b]A negative slope was considered adverse for this variable.

Note: NS or ns: Not significant ($p > 0.05$).

     C: Continuous form of dependent variable.

     D: Discrete form of dependent variable.

     The p-value was given if $p \leq 0.05$. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

     A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

18.4.3   Model 3: Categorized Dioxin Analysis

The adjusted Model 3 analysis revealed significantly higher mean TSH values and a longer time to develop diabetes among Ranch Hands in the background dioxin category than among Comparisons. Ranch Hands in the low dioxin category displayed a significantly higher mean LH value than Comparisons. More Ranch Hands in the high dioxin category required insulin to control diabetes than Comparisons. The results of all unadjusted and adjusted Model 3 analyses are summarized in Table 18-45.

Table 18-45. Summary of Categorized Dioxin Analysis (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Past Thyroid Disease (D)	ns	ns	ns	ns
Composite Diabetes Indicator (2002 AFHS diabetes definition) (D)	ns	NS	NS	NS
Composite Diabetes Indicator (pre-2002 AFHS diabetes definition) (D)	ns	NS	NS	NS
Diabetic Control (D) (2002 AFHS diabetes definition)				
No Treatment vs. Nondiabetic	ns	NS	ns	NS
Diet and Exercise vs. Nondiabetic	ns	NS	ns	ns
Oral Hypoglycemics vs. Nondiabetic	ns	NS	NS	NS
Requiring Insulin vs. Nondiabetic	ns	ns	p=0.037 (2.11)	ns
Diabetic Control (D) (pre-2002 AFHS diabetes definition)				
No Treatment vs. Nondiabetic	ns	NS	ns	NS
Diet and Exercise vs. Nondiabetic	ns	NS	ns	ns
Oral Hypoglycemics vs. Nondiabetic	ns	NS	NS	NS
Requiring Insulin vs. Nondiabetic	ns	ns	p=0.038 (2.11)	ns
Time to Diabetes Onset (2002 AFHS diabetes definition) (C)[a]	p=0.017 (0.67)	NS	NS	NS
Time to Diabetes Onset (pre-2002 AFHS diabetes definition) (C)[a]	p=0.016 (0.69)	NS	NS	NS
Physical Examination				
Thyroid Gland (D)	ns	ns	ns	p=0.044 (*)
Testicular Examination (D)	NS	NS	NS	NS
Laboratory				
TSH (C)	p=0.007 (0.174)	NS	NS	NS
TSH (D)				
Low vs. Normal	ns	ns	ns	ns
High vs. Normal	NS	NS	NS	NS
Free T_4 (C)[b]	NS	NS	NS	NS
Free T_4 (D)	ns	ns	ns	ns
Anti-Thyroid Antibodies (D)	ns	NS	ns	NS
Fasting Glucose (C)	ns	NS	NS	NS
Fasting Glucose (D)	NS	NS	NS	NS
2-hour Postprandial Glucose (C)	NS	NS	ns	ns
2-hour Postprandial Glucose (D)	NS	NS	ns	NS
2-hour Postprandial Urinary Glucose (D)	NS	ns	NS	NS
Fasting Insulin (C)	ns	NS	p=0.009 (1.21)	p=0.006 (0.96)
Fasting Insulin (D)				
Low vs. Normal	ns	ns	ns	ns
High vs. Normal	NS	NS	p=0.009 (1.96)	p=0.018 (1.67)

| | UNADJUSTED | | | |
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
2-hour Postprandial Insulin (C)	ns	NS	NS	NS
2-hour Postprandial Insulin (D)				
Low vs. Normal	NS	ns	NS	ns
High vs. Normal	ns	NS	NS	NS
Hemoglobin A1c (C)	ns	ns	NS	NS
Hemoglobin A1c (D)	ns	ns	NS	NS
C-peptide (C)	ns	NS	ns	NS
C-peptide (D)	ns	NS	ns	NS
Proinsulin (C)	ns	NS	NS	NS
Proinsulin (D)	ns	NS	NS	NS
GADA (D)	ns	NS	ns	ns
Total Testosterone (C)[b]	ns	ns	NS	ns
Total Testosterone (D)	NS	NS	NS	NS
Free Testosterone (C)[b]	ns	ns	NS	NS
Free Testosterone (D)	NS	NS	ns	NS
Estradiol (C)	NS	NS	ns	NS
Estradiol (D)	NS	ns	NS	ns
LH (C)	NS	p=0.006 (0.61)	ns	NS
LH (D)	ns	ns	ns	ns
FSH (C)	NS	p=0.019 (0.72)	ns	NS
FSH (D)	NS	NS	ns	ns

[a]A hazard ratio was used. A hazard ratio greater than 1.0 implies a shorter time to the onset of diabetes for Ranch Hands than for Comparisons. A hazard ratio less than 1.0 implies a longer time to the onset of diabetes for Ranch Hands than for Comparisons.

[b]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse for this variable.

*: Relative risk was not able to be calculated. Zero Ranch Hands in the high dioxin category and 24 Comparisons had an abnormal thyroid gland.

Note: NS or ns: Not significant (p>0.05).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

      The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

      A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

Table 18-45. Summary of Categorized Dioxin Analysis (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons) (Continued)

	ADJUSTED			
Variable	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Medical Records				
Past Thyroid Disease (D)	ns	ns	ns	ns
Composite Diabetes Indicator (2002 AFHS diabetes definition) (D)	ns	NS	NS	NS
Composite Diabetes Indicator (pre-2002 AFHS diabetes definition) (D)	ns	ns	NS	NS
Diabetic Control (2002 AFHS diabetes definition) (D)				
No Treatment vs. Nondiabetic	ns	NS	ns	NS
Diet and Exercise vs. Nondiabetic	ns	ns	ns	ns
Oral Hypoglycemics vs. Nondiabetic	ns	NS	NS	NS
Requiring Insulin vs. Nondiabetic	ns	ns	p=0.016 (2.66)	NS
Diabetic Control (pre-2002 AFHS diabetes definition) (D)				
No Treatment vs. Nondiabetic	ns	NS	ns	ns
Diet and Exercise vs. Nondiabetic	ns	ns	ns	ns
Oral Hypoglycemics vs. Nondiabetic	ns	NS	NS	NS
Requiring Insulin vs. Nondiabetic	ns	ns	p=0.017 (2.64)	ns
Time to Diabetes Onset (2002 AFHS diabetes definition) (C)[a]	p=0.030 (0.69)	NS	NS	NS
Time to Diabetes Onset (pre-2002 AFHS diabetes definition) (C)[a]	p=0.030 (0.71)	NS	NS	NS
Physical Examination				
Thyroid Gland (D)	ns	ns	--	--
Testicular Examination (D)	NS	ns	NS	NS
Laboratory				
TSH (C)	p=0.036 (0.122)	NS	NS	NS
TSH (D)				
Low vs. Normal	--	--	ns	--
High vs. Normal	NS	NS	NS	NS
Free T_4 (C)[b]	NS	NS	NS	NS
Free T_4 (D)	ns	ns	ns	ns
Anti-Thyroid Antibodies (D)	ns	NS	NS	NS
Fasting Glucose (C)	NS	NS	NS	NS
Fasting Glucose (D)	NS	NS	NS	NS
2-hour Postprandial Glucose (C)	NS	ns	ns	ns
2-hour Postprandial Glucose (D)	NS	NS	ns	ns
2-hour Postprandial Urinary Glucose (D)	NS	ns	ns	ns
Fasting Insulin (C)	NS	NS	NS	NS
Fasting Insulin (D)				
Low vs. Normal	ns	ns	ns	ns
High vs. Normal	NS	NS	NS	NS

Table 18-45. Summary of Categorized Dioxin Analysis (Model 3) for Endocrine Variables (Ranch Hands vs. Comparisons) (Continued)

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
2-hour Postprandial Insulin (C)	ns	ns	ns	ns
2-hour Postprandial Insulin (D)				
Low vs. Normal	NS	ns	NS	NS
High vs. Normal	ns	ns	ns	ns
Hemoglobin A1c (C)	ns	NS	NS	NS
Hemoglobin A1c (D)	ns	NS	NS	NS
C-peptide (C)	NS	NS	ns	NS
C-peptide (D)	NS	NS	ns	NS
Proinsulin (C)	ns	NS	NS	NS
Proinsulin (D)	NS	NS	NS	NS
GADA (D)	--	NS	ns	ns
Total Testosterone (C)[b]	NS	NS	NS	NS
Total Testosterone (D)	NS	ns	NS	NS
Free Testosterone (C)[b]	ns	NS	ns	NS
Free Testosterone (D)	NS	ns	NS	NS
Estradiol (C)	NS	ns	NS	ns
Estradiol (D)	NS	ns	NS	ns
LH (C)	NS	p=0.015 (0.51)	ns	NS
LH (D)	ns	ns	ns	ns
FSH (C)	NS	NS	ns	NS
FSH (D)	ns	NS	ns	ns

[a]A hazard ratio was used. A hazard ratio greater than 1.0 implies a shorter time to the onset of diabetes for Ranch Hands than for Comparisons. A hazard ratio less than 1.0 implies a longer time to the onset of diabetes for Ranch Hands than for Comparisons.

[b]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse for this variable.

--: Analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
     C: Continuous form of dependent variable.
     D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

18.4.4 Model 4: 1987 Dioxin Level Analysis

The Model 4 analyses showed a significant positive association between 1987 dioxin and diabetes. A significant positive association between 1987 dioxin and the percentage of Ranch Hands taking oral hypoglycemics was seen, as was a significant positive association between 1987 dioxin and the percentage of Ranch Hands requiring insulin to control diabetes. Time to diabetes onset decreased as 1987 dioxin level increased. The prevalence of 2-hour postprandial urinary glucose decreased as the 1987 dioxin level increased. The percentage of abnormally high hemoglobin A1c values increased as the 1987 dioxin level increased. All results for Model 4 unadjusted and adjusted analyses are summarized in Table 18-46.

Table 18-46. Summary of 1987 Dioxin Analysis (Model 4) for Endocrine Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Past Thyroid Disease (D)	ns	ns
Composite Diabetes Indicator (2002 AFHS diabetes definition) (D)	p<0.001 (1.27)	p=0.001 (1.29)
Composite Diabetes Indicator (pre-2002 AFHS diabetes definition) (D)	p<0.001 (1.24)	p=0.001 (1.27)
Diabetic Control (2002 AFHS diabetes definition) (D)		
No Treatment vs. Nondiabetic	NS	NS
Diet and Exercise vs. Nondiabetic	NS	NS
Oral Hypoglycemics vs. Nondiabetic	p<0.001 (1.32)	p=0.006 (1.32)
Requiring Insulin vs. Nondiabetic	p=0.007 (1.43)	p=0.021 (1.53)
Diabetic Control (pre-2002 AFHS diabetes definition) (D)		
No Treatment vs. Nondiabetic	NS	NS
Diet and Exercise vs. Nondiabetic	NS	ns
Oral Hypoglycemics vs. Nondiabetic	p<0.001 (1.32)	p=0.005 (1.32)
Requiring Insulin vs. Nondiabetic	p=0.007 (1.43)	p=0.019 (1.54)
Time to Diabetes Onset (2002 AFHS diabetes definition) (C)[a]	p<0.001 (1.25)	p<0.001 (1.28)
Time to Diabetes Onset (pre-2002 AFHS diabetes definition) (C)[a]	p<0.001 (1.23)	p<0.001 (1.26)
Physical Examination		
Thyroid Gland (D)	ns	ns
Testicular Examination (D)	NS	NS
Laboratory		
TSH (C)	ns	ns
TSH (D)		
Low vs. Normal	NS	NS
High vs. Normal	ns	ns
Free T_4 (C)[b]	ns	NS
Free T_4 (D)	ns	ns
Anti-Thyroid Antibodies (D)	ns	NS
Fasting Glucose (C)	p<0.001 (0.016)	NS
Fasting Glucose (D)	p=0.032 (1.12)	NS
2-hour Postprandial Glucose (C)	ns	ns
2-hour Postprandial Glucose (D)	ns	ns
2-hour Postprandial Urinary Glucose (D)	ns	p=0.040 (0.87)

Table 18-46. Summary of 1987 Dioxin Analysis (Model 4) for Endocrine Variables (Ranch Hands Only) (Continued)

Variable	Unadjusted	Adjusted
Fasting Insulin (C)	p<0.001 (0.077)	NS
Fasting Insulin (D)		
Low vs. Normal	p=0.002 (0.76)	NS
High vs. Normal	p<0.001 (1.34)	NS
2-hour Postprandial Insulin (C)	p=0.004 (0.058)	ns
2-hour Postprandial Insulin (D)		
Low vs. Normal	ns	ns
High vs. Normal	p=0.009 (1.15)	NS
Hemoglobin A1c (C)	p=0.023 (0.023)	NS
Hemoglobin A1c (D)	p=0.005 (1.38)	p=0.031 (1.35)
C-peptide (C)	NS	ns
C-peptide (D)	ns	ns
Proinsulin (C)	NS	ns
Proinsulin (D)	NS	ns
GADA (D)	NS	NS
Total Testosterone (C)[b]	ns	NS
Total Testosterone (D)	NS	NS
Free Testosterone (C)[b]	ns	ns
Free Testosterone (D)	NS	NS
Estradiol (C)	NS	NS
Estradiol (D)	ns	ns
LH (C)	ns	ns
LH (D)	ns	ns
FSH (C)	ns	NS
FSH (D)	ns	NS

[a] A hazard ratio was used. A hazard ratio greater than 1.0 implies that onset of diabetes becomes shorter as 1987 dioxin increases. A hazard ratio less than 1.0 implies that onset of diabetes becomes longer as 1987 dioxin increases.
[b] A negative slope was considered adverse for this variable.

Note: NS or ns: Not significant (p>0.05).
     C: Continuous form of dependent variable.
     D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

18.4.5 Summary of Significant Results

Table 18-47 summarizes the significant results (p≤0.05) for the adjusted analyses that were performed for the endocrinology assessment. The dependent variable and its table reference are listed along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and is explained in footnotes.

Table 18-47. Summary of Results from Significant Adjusted Analyses in the Endocrinology Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Composite Diabetes Indicator (2002 AFHS diabetes definition) (18-4)	4	All RH: 1987 Dioxin	0.001	1.29 (1.10,1.51)	Low: 9.6% Medium: 20.2% High: 24.9%	(a)
Composite Diabetes Indicator (pre-2002 AFHS diabetes definition) (18-5)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.010	1.34 (1.07,1.68)	Low: 22.1% Medium: 27.5% High: 27.0%	(b)
	4	All RH: 1987 Dioxin	0.001	1.27 (1.09,1.47)	Low: 12.3% Medium: 22.1% High: 27.6%	(a)
Diabetic Control (2002 AFHS diabetes definition) (18-6)	2	RH (1987 dioxin >10 ppt): Initial Dioxin – Requiring Insulin vs. Nondiabetic	<0.001	2.78 (1.61,4.82)	Low: 0.7% Medium: 2.1% High: 7.1%	(b)
	3	High RH vs. C - Requiring Insulin vs. Nondiabetic	0.016	2.66 (1.20,5.87)	RH: 5.6% C: 2.5%	(c)
	4	All RH: 1987 Dioxin – Oral Hypoglycemics vs. Nondiabetic	0.006	1.32 (1.08,1.60)	Low: 3.9% Medium: 11.2% High: 14.0%	(a)
	4	All RH: 1987 Dioxin – Requiring Insulin vs. Nondiabetic	0.021	1.53 (1.07,2.19)	Low: 1.9% Medium: 1.2% High: 5.1%	(a)

Table 18-47. Summary of Results from Significant Adjusted Analyses in the Endocrinology Assessment (Continued)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Diabetic Control (pre-2002 AFHS diabetes definition) (18-7)	1	RH vs. C, Enlisted Groundcrew: No Treatment vs. Nondiabetic	0.037	0.51 (0.27,0.96)	RH: 4.2% C: 7.8%	(d)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin - Requiring Insulin vs. Nondiabetic	<0.001	2.90 (1.68,5.01)	Low: 0.7% Medium: 2.1% High: 7.1%	(b)
	3	High RH vs. C - Requiring Insulin vs. Nondiabetic	0.017	2.64 (1.19,5.83)	RH: 5.6% C: 2.5%	(c)
Diabetic Control (pre-2002 AFHS diabetes definition) (18-7) (continued)	4	All RH: 1987 Dioxin – Oral Hypoglycemics vs. Nondiabetic	0.005	1.32 (1.09,1.61)	Low: 3.9% Medium: 11.2% High: 14.0%	(a)
	4	All RH: 1987 Dioxin – Requiring Insulin vs. Nondiabetic	0.019	1.54 (1.07,2.21)	Low: 1.9% Medium: 1.2% High: 5.1%	(a)
Time to Diabetes Onset (2002 AFHS diabetes definition) (18-8)[a]	3	Background RH vs. C	0.030	0.69 (0.49,0.96)	RH: 33.17 years C: 28.41 years	(e)
	4	All RH: 1987 Dioxin	<0.001	1.28 (1.12,1.46)	Low: 34.42 years Medium: 26.75 years High: 23.67 years	(f)
Time to Diabetes Onset (pre-2002 AFHS diabetes definition) (18-9)[a]	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.033	1.21 (1.02,1.45)	Low: 25.75 years Medium: 25.91 years High: 21.58 years	(g)
	3	Background RH vs. C	0.030	0.71 (0.52,0.97)	RH: 33.08 years C: 28.41 years	(e)
	4	All RH: 1987 Dioxin	<0.001	1.26 (1.12,1.43)	Low: 33.50 years Medium: 26.75 years High: 23.67 years	(f)
TSH (18-12)	1	RH vs. C, All	0.024	0.096	RH: 1.653 µIU/mL C: 1.557 µIU/mL	(h)
	1	RH vs. C, Officer	0.009	0.189	RH: 1.778 µIU/mL C: 1.589 µIU/mL	(h)
	3	Background RH vs. C	0.036	0.122	RH: 1.682 µIU/mL C: 1.560 µIU/mL	(i)
Free T_4 (18-14)[b]	1	RH vs. C, Enlisted Flyer	0.002	0.061	RH: 1.115 ng/dL C: 1.054 ng/dL	(h)
Free T_4 (18-15)	1	RH vs. C, Enlisted Flyer	0.026	0.37 (0.15,0.89)	RH: 5.6% C: 13.8%	(d)
2-hour Postprandial Glucose (18-19)	1	RH vs. C, Enlisted Groundcrew	0.006	-7.4	RH: 107.4 mg/dL C: 114.8 mg/dL	(h)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
2-hour Postprandial Urinary Glucose (18-21)	1	RH vs. C, Officer	0.050	1.48 (1.00,2.20)	RH: 23.6% C: 17.7%	(d)
	4	All RH: 1987 Dioxin	0.040	0.87 (0.76,0.99)	Low: 27.9% Medium: 25.5% High: 28.3%	(a)
Fasting Insulin (18-22)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.014	0.056 (0.023)	Low: 11.84 μIU/mL Medium: 11.86 μIU/mL High: 13.01 μIU/mL	(j)
Fasting Insulin (18-23)	2	RH (1987 dioxin >10 ppt): Initial Dioxin - Abnormal High vs. Normal	0.006	1.54 (1.13,2.09)	Low: 6.4% Medium: 9.9% High: 13.5%	(b)
2-hour Postprandial Insulin (18-24)	1	RH vs. C, Enlisted Groundcrew	0.033	-7.64	RH: 61.83 μIU/mL C: 69.47 μIU/mL	(h)
2-hour Postprandial Insulin (18-25)	1	RH vs. C, Enlisted Groundcrew – Abnormal High vs. Normal	0.043	0.70 (0.50,0.99)	RH: 49.1% C: 56.2%	(d)
Hemoglobin A1c (18-27)	4	All RH: 1987 Dioxin	0.031	1.35 (1.01,1.80)	Low: 48.0% Medium: 62.0% High: 73.4%	(a)
C-peptide (18-28)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.017	-0.091 (0.038)	Low: 3.69 ng/mL Medium: 4.17 ng/mL High: 2.88 ng/mL	(j)
Free Testosterone (18-36)	1	RH vs. C, Officer	0.039	1.87 (1.03,3.39)	RH: 9.2% C: 5.0%	(d)
LH (18-39)	1	RH vs. C, Officer	0.040	0.40	RH: 4.49 mIU/mL C: 4.09 mIU/mL	(h)
	3	Low RH vs. C	0.015	0.51	RH: 4.81 mIU/mL C: 4.30 mIU/mL	(i)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal was presented for each of three initial dioxin categories.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(e): Continuous variable: adjusted hazard ratio and 95% confidence interval were presented; 10th percentile of distribution of time to onset of diabetes was presented for each dioxin category in contrast.

(f): Continuous variable: adjusted hazard ratio and 95% confidence interval were presented for a twofold increase in 1987 dioxin; 10th percentile of distribution of time to onset of diabetes was presented for each of three 1987 dioxin categories.

(g): Continuous variable: adjusted hazard ratio and 95% confidence interval were presented for a twofold increase in initial dioxin; 10th percentile of distribution of time to onset of diabetes was presented for each of three initial dioxin categories.

(h): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each exposure group in contrast.

(i): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each dioxin category in contrast.

(j): Continuous variable: slope and standard error were presented and were based on natural logarithm of dependent variable versus $\log_2$ (initial dioxin); adjusted means were presented for each of three initial dioxin categories.

[a]A smaller group mean or decreasing mean time to onset values as dioxin increased was considered adverse for this variable.
[b]A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: RH = Ranch Hand.
        C = Comparison.

   Model 2:   Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt).

   Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
              Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
              High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

   Model 4:   Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

18.5   CONCLUSION

A number of significant adverse associations were found between dioxin levels and diabetes, glucose, insulin, gonadotropins, and thyroid hormones. These were not specific to a particular statistical model or to the form of the outcome variable (continuous or discrete) and are summarized below by statistical model.

With regard to group contrasts, Ranch Hands had a significantly higher mean TSH than Comparisons, primarily due to a significantly increased mean among Ranch Hand officers. Ranch Hand officers also exhibited a significantly increased mean LH, a significantly increased risk of abnormal 2-hour postprandial urinary glucose, and abnormal free testosterone.

Analyses using the extrapolated initial dioxin level found that mean fasting insulin and the risk of diabetes requiring insulin control increased significantly with initial dioxin. C-peptide and time to diabetes onset decreased as initial dioxin increased.

Analyses based on dioxin category found that the risk of diabetes requiring insulin control was significantly increased in the high dioxin category.

Analyses based on the 1987 dioxin level revealed an increase in the risk of diabetes requiring oral hypoglycemic or insulin control as 1987 dioxin levels increased. Time to diabetes onset decreased as 1987 dioxin levels increased. The risk of an abnormally high hemoglobin A1c increased with 1987 dioxin levels.

Some findings appeared to conflict with these, such as a decrease in the risk of 2-hour postprandial urinary glucose abnormalities with 1987 dioxin levels.

In summary, these findings appear consistent with the previously noted association between Type 2 diabetes and dioxin in Ranch Hand veterans. Increased risks of diabetes requiring insulin control were found with initial dioxin, in the high dioxin category, and with 1987 dioxin levels. In contrast, associations between dioxin levels and thyroid or gonadal hormone abnormalities were unlikely to be clinically important.

REFERENCES

1. Institute of Medicine. 2000. Herbicide/Dioxin Exposure and Type 2 Diabetes. National Academy Press: Washington, DC.

2. Gress, T.W., F.J. Nieto, E. Shahar, M.R. Wofford, and F.L. Brancati. 2000. Hypertension and antihypertensive therapy as risk factors for type 2 diabetes mellitus. Atherosclerosis Risk in Communities Study. *New England Journal of Medicine* 342(13):905-12.

3. Longnecker, M.P., and J.L. Daniels. 2001. Environmental contaminants as etiologic factors for diabetes. *Environmental Health Perspectives* 109(Suppl 6):871-6.

4. Michalek, J.E., A.J. Rahe, and C.A. Boyle. 1998. Paternal dioxin and the sex of children fathered by veterans of Operation Ranch Hand. *Epidemiology* 9:474-5.

5. Michalek, J.E., A.J. Rahe, and C.A. Boyle. 1998. Paternal dioxin, preterm birth, intrauterine growth retardation, and infant death. *Epidemiology* 9:161-7.

6. Okey, A.B., D.S. Riddick, and P.A. Harper. 1994. The Ah receptor: Mediator of the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. *Toxicology Letters* 70:1-22.

7. Lucier, G. 1991. Humans are sensitive species to some of the biochemical effects of structural analogs of dioxin. *Environmental Toxicology and Chemistry* 10:727-35.

8. Wang, X., R. Rosengren, V. Morrison, and S. Safe. 1992. Characterization of the human Ah receptor. *Chemosphere* 25:997-1000.

9. Cuthill, S., A. Wilhelmsson, G.G. Mason, M. Gillner, L. Poellinger, and J.A. Gustafsson. 1988. The dioxin receptor: A comparison with the glucocorticoid receptor. *Journal of Steroid Biochemistry and Molecular Biology* 30:277-80.

10. Potter, C.L., I.G. Sipes, and D.H. Russell. 1983. Hypothyroxinemia and hypothermia in rats in response to 2,3,7,8-tetrachlorodibenzo-p-dioxin administration. *Toxicology and Applied Pharmacology* 69:89-95.

11. Bastomsky, C.H. 1977. Enhanced thyroxine metabolism and high uptake goiters in rats after a single dose of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Endocrinology* 101:292-6.

12. McKinney, J.D., J. Fawkes, S. Jordan, K. Chae, S. Oatley, R.E. Coleman, and W. Briner. 1985. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) as a potent and persistent thyroxine agonist: A mechanistic model for toxicity based on molecular reactivity. *Environmental Health Perspectives* 61:41-53.

13. Rozman, K., T. Rozman, E. Scheufler, T. Pazdernik, and H. Greim. 1985. Thyroid hormones modulate the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Journal of Toxicology and Environmental Health* 16:481-91.

14. Roth, W., R. Voorman, and S.D. Aust. 1988. Activity of thyroid hormone-inducible enzymes following treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacology* 92:65-74.

15. Gorski, J.R., G. Muzi, L.W. Weber, D.W. Pereira, R.J. Arceo, M.J. Iatropoulos, and K. Rozman. 1988. Some endocrine and morphological aspects of the acute toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicologic Pathology* 16:313-20.

16. van der Plas, S.A., I. Lutkeschipholt, B. Spenkelink, and A. Brouwer. 2001. Effects of subchronic exposure to complex mixtures of dioxin-like and non-dioxin-like polyhalogenated aromatic compounds on thyroid hormone and vitamin A levels in female Sprague-Dawley rats. *Toxicological Sciences* 59:92-100.

17. Nishimura, N., J. Yonemoto, Y. Miyabara, M. Sato, and C. Tohyama. 2003. Rat thyroid hyperplasia induced by gestational and lactational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Endocrinology* 144:2075-83.

18. Pohjanvirta, R., T. Kulju, A.F. Morselt, R. Tuominen, R. Juvonen, K. Rozman, P. Mannisto, Y. Collan, E.L. Sainio, and J. Tuomisto. 1989. Target tissue morphology and serum biochemistry following 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) exposure in a TCDD-susceptible and a TCDD-resistant rat strain. *Fundamental and Applied Toxicology* 12:698-712.

19. Henry, E.C., and T.A. Gasiewicz. 1987. Changes in thyroid hormones and thyroxine glucuronidation in hamsters compared with rats following treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacolog*y 89:65-74.

20. Fan, F., and K.K. Rozman. 1995. Short- and long-term biochemical effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin in female Long-Evans rats. *Toxicology Letters* 75:209-16.

21. Sewall, C.H., N. Flagler, J.P. Vanden Heuvel, G.C. Clark, A.M. Tritscher, R.M. Maronpot, and G.W. Lucier. 1995. Alterations in thyroid function in female Sprague-Dawley rats following chronic treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacology* 132:237-44.

22. Enan, E., and F. Matsumura. 1994. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-induced changes in glucose transporting activity in guinea pigs, mice, and rats in vivo and in vitro. *Journal of Biochemical Toxicology* 9:97-106.

23. Brewster, D.W., and F. Matsumura. 1984. TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) reduces lipoprotein lipase activity in the adipose tissue of the guinea pig. *Biochemical and Biophysical Research Communications* 122:810-7.

24. Enan, E., P.C. Liu, and F. Matsumura. 1992. TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) causes reduction in glucose uptake through glucose transporters on the plasma membrane of the guinea pig adipocyte. *Journal of Environmental Science and Health* 27:495-510.

25. Enan, E., P.C. Liu, and F. Matsumura. 1992. 2,3,7,8-Tetrachlorodibenzo-p-dioxin causes reduction of glucose transporting activities in the plasma membranes of adipose tissue and pancreas from the guinea pig. *Journal of Biological Chemistry* 267:19785-91.

26. Enan, E., and F. Matsumura. 1993. 2,3,7,8-Tetrachlorodibenzo-p-dioxin induced alterations in protein phosphorylation in guinea pig adipose tissue. *Journal of Biochemical Toxicology* 8:89-99.

27. Gasiewicz, T.A., M.A. Holscher, and R.A. Neal. 1980. The effect of total parenteral nutrition on the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the rat. *Toxicology and Applied Pharmacology* 54:469-88.

28. Stahl, B.U., D.G. Beer, L.W. Weber, and K. Rozman. 1993. Reduction of hepatic phosphoenolpyruvate carboxykinase (PEPCK) activity by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is due to decreased mRNA levels. *Toxicology* 79:81-95.

29. Gorski, J.R., M. Lebofsky, and K. Rozman. 1988. Corticosterone decreases toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in hypophysectomized rats. *Journal of Toxicology and Environmental Health* 25:349-60.

30. Bestervelt, L.L., C.J. Nolan, Y. Cai, P. Maimansomsuk, C.A. Mousigian, and W.N. Piper. 1991. Tetrachlorodibenzo-p-dioxin alters rat hypothalamic endorphin and mu opioid receptors. *Neurotoxicology and Teratology* 13:495-7.

31. Russell, D.H., A.R. Buckley, G.N. Shah, I.G. Sipes, D.E. Blask, and B. Benson. 1988. Hypothalamic site of action of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicology and Applied Pharmacology* 94:496-502.

32. Bestervelt, L.L., Y. Cai, D.W. Piper, C.J. Nolan, J.A. Pitt, and W.N. Piper. 1993. TCDD alters pituitary-adrenal function I: Adrenal responsiveness to exogenous ACTH. *Neurotoxicology and Teratology* 15:365-7.

33. Bestervelt, L.L., D.W. Piper, J.A. Pitt, and W.N. Piper. 1994. Lipid peroxidation in the adrenal glands of male rats exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicology Letters* 70:139-45.

34. Prokipcak, R.D., L.E. Faber, and A.B. Okey. 1989. Characterization of the Ah receptor for 2,3,7,8-tetrachlorodibenzo-p-dioxin: Use of chemical crosslinking and a monoclonal antibody directed against a 59-kDa protein associated with steroid receptors. *Archives of Biochemistry and Biophysics* 274:648-58.

35. Couture, L.A., B.D. Abbott, and L.S. Birnbaum. 1990. A critical review of the developmental toxicity and teratogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin: recent advances toward understanding the mechanism. *Teratology* 42:619-27.

36. Mattison, D.R., M.S. Nightingale, and E.K. Silberger. 1984. Reproductive toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin. In: Public Health Risks of the Dioxins. W.W. Lowrance, ed. Kaufman Inc.: Los Altos, CA.

37. Dickerson, R., L. Johnson, and S. Safe. 1989. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on androgen function in the male rat. *Toxicologist* 9:32.

38. Johnson, L., R. Dickerson, S.H. Safe, C.L. Nyberg, R.P. Lewis, and T.H. Welsh, Jr. 1992. Reduced Leydig cell volume and function in adult rats exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin without a significant effect on spermatogenesis. *Toxicology* 76:103-18.

39. Mably, T.A., R.W. Moore, and R.E. Peterson. 1992. In utero and lactational exposure of male rats to 2,3,7,8-tetrachlorodibenzo-p-dioxin, 1. Effects on androgenic status. *Toxicology and Applied Pharmacolog*y 114:97-107.

40. Mably, T.A., D.L. Bjerke, R.W. Moore, A. Gendron-Fitzpatrick, and R.E. Peterson. 1992. In utero and lactational exposure of male rats to 2,3,7,8-tetrachlorodibenzo-p-dioxin, 3: Effects on spermatogenesis and reproductive capability. *Toxicology and Applied Pharmacology* 114:118-26.

41. Latchoumycandane, C., K.C. Chitra, and P.P. Mathur. 2002. The effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin on the antioxidant system in mitochondrial and microsomal fractions of rat testis. *Toxicology* 171:127-35.

42. Yonemoto, J. 2003. The effects of dioxin on reproduction and development. *Industrial Health* 2000:259-68.

43. Kakeyama, M., and C. Tohyama. 2003. Developmental neurotoxicity of dioxin and its related compounds. *Industrial Health* 41:215-30.

44. Moore, R.W., C.L. Potter, H.M. Theobald, J.A. Robinson, and R.E. Peterson. 1985. Androgenic deficiency in male rats treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicology and Applied Pharmacology* 79:99-111.

45. Moore, R.W., and R.E. Peterson. 1988. Androgen catabolism and excretion in 2,3,7,8-tetrachlorodibenzo-p-dioxin-treated rats. *Biochemical Pharmacology* 37:560-2.

46. Moore, R.W., J.A. Parsons, R.C. Bookstaff, and R.E. Peterson. 1989. Plasma concentrations of pituitary hormones in 2,3,7,8-tetrachlorodibenzo-p-dioxin-treated male rats. *Journal of Biochemical Toxicology* 4:165-72.

47. Bookstaff, R.C., R.W. Moore, and R.E. Peterson. 1990. 2,3,7,8-tetrachlorodibenzo-p-dioxin increases the potency of androgens and estrogens as feedback inhibitors of luteinizing hormone secretion in male rats. *Toxicology and Applied Pharmacology* 104:212-24.

48. Bookstaff, R.C., F. Kamel, R.W. Moore, D.L. Bjerke, and R.E. Peterson. 1990. Altered regulation of pituitary gonadotropin-releasing hormone (GnRH) receptor number and pituitary responsiveness to GnRH in 2,3,7,8-tetrachlorodibenzo-p-dioxin-treated male rats. *Toxicology and Applied Pharmacology* 105:78-92.

49. Zober, A., M.G. Ott, and P. Messerer. 1994. Morbidity follow up study of BASF employees exposed to 2,3,7, 8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

50. Ott, M.G., A. Zober, and C. Germann. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.

51. Calvert, G.M., M.H. Sweeney, J. Deddens, and D.K. Wall. 1999. Evaluation of diabetes mellitus, serum glucose, and thyroid function among United States workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Occupational and Environmental Medicine* 56:270-6.

52. Pavuk, M., A. Schecter, F.Z. Akhtar, and J.E. Michalek. 2003. Serum 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) levels and thyroid function in Air Force veterans of the Vietnam War. *Annals of Epidemiology* 13:335-43.

53. Institute of Medicine. 2003. Veterans and Agent Orange: Update 2002. National Academy Press: Washington, DC.

54. Pazderova-Vejlupkova, J., E. Lukas, M. Nemcova, J. Pickova, and L. Jirasek. 1981. The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. *Archives of Environmental Health* 36:5-11.

55. Steenland, K., L. Piacitelli, J. Deddens, M. Fingerhut, and L.I. Chang. 1999. Cancer, heart disease, and diabetes in workers exposed to 2,3,7,8- tetrachlorodibenzo-p-dioxin. *Journal of the National Cancer Institute* 91(9):779-86.

56. Sweeney, M.H., G.M. Calvert, G.A. Egeland, M.A. Fingerhut, W.E. Halperin, and L.A. Piacitelli. 1997. Review and update of the results of the NIOSH medical study of workers exposed to chemicals contaminated with 2,3,7,8-tetrachlorodibenzodioxin. *Teratogenesis, Carcinogenesis, and Mutagenesis* 17:241-7.

57. Vena, J., P. Boffetta, H. Becher, T. Benn, H.B. Bueno-de-Mesquita, D. Coggon, D. Colin, D. Flesch-Janys, L. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, N. Pearce, A.C. Pesatori, R. Saracci, K. Steenland, and M. Kogevinas. 1998. Exposure to dioxin and nonneoplastic mortality in the expanded IARC international cohort study of phenoxy herbicide and chlorophenol production workers and sprayers. *Environmental Health Perspectives* 106(Suppl 2):645-53.

58. Pesatori, A.C., C. Zocchetti, S. Guercilena, D. Consonni, D. Turrini, and P.A. Bertazzi. 1998. Dioxin exposure and non-malignant health effects: a mortality study. *Occupational and Environmental Medicine* 55:126-31.

59. Henriksen, G.L., N.S. Ketchum, J.E. Michalek, and J.A. Swaby. 1997. Serum dioxin and diabetes mellitus in veterans of Operation Ranch Hand. *Epidemiology* 8:252-8.

60. Michalek, J.E., F.Z. Akhtar, and J.L. Kiel. 1999. Serum dioxin, insulin, fasting glucose, and sex hormone-binding globulin in veterans of Operation Ranch Hand. *Journal of Clinical Endocrinology and Metabolism* 84:1540-3.

61. Longnecker, M.P., and J.E. Michalek. 2000. Serum dioxin level in relation to diabetes mellitus among Air Force veterans with background levels of exposure. *Epidemiology* 11:44-8.

62. Kim, J.S., H.S. Lim, S.I. Cho, H.K. Cheong, and M.K. Lim. 2003. Impact of Agent Orange exposure among Korean Vietnam veterans. *Industrial Health* 41:149-57.

63. Pesatori, A.C., D. Consonni, S. Bachetti, C. Zocchetti, M. Bonzini, A. Baccarelli, and P.A. Bertazzi. 2003. Short- and long-term morbidity and mortality in the population exposed to dioxin after the "Seveso Accident." *Industrial Health* 41:127-138.

64. Michalek, J.E. 1998. Author's reply: Dioxin and diabetes mellitus. *Epidemiology* 9:359-60.

65. Michalek, J.E., N.S. Ketchum, and R.C. Tripathi. 2003. Diabetes mellitus and 2,3,7,8-tetrachlorodibenzo-p-dioxin elimination in veterans of Operation Ranch Hand. *Journal of Toxicology and Environmental Health* 66:211-21.

66. Institute of Medicine. 2001. Veterans and Agent Orange: Update 2000. National Academy Press: Washington, DC.

67. Egeland, G.M., M.H. Sweeney, M.A. Fingerhut, K.K. Wille, T.M. Schnorr, and W.E. Halperin. 1994. Total serum testosterone and gonadotropins in workers exposed to dioxin. *American Journal of Epidemiology* 139:272-81.

68. Henriksen, G.L., J.E. Michalek, J.A. Swaby, and A.J. Rahe. 1996. Serum dioxin, testosterone, and gonadotropins in veterans of Operation Ranch Hand. *Epidemiology* 7:352-7.

69. Henriksen, G.L., and J.E. Michalek. 1996. Serum dioxin, testosterone, and gonadotropins in veterans of Operation Ranch Hand. *Epidemiology* 7:454-5.

70. Mocarelli, P., P.M. Gerthoux, E. Ferrari, D.G. Patterson, Jr., S.M. Kieszak, P. Brambilla, N. Vincoli, S. Signorini, P. Tramacere, V. Carreri, E.J. Sampson, W.E. Turner, and L.L. Needham. 2000. Paternal concentrations of dioxin and sex ratio of offspring. *Lancet* 355:1858-63.

71. Schnorr, T.M., C.C. Lawson, E.A. Whelan, D.A. Dankovic, J.A. Deddens, L.A. Piacitelli, J. Reefhuis, M.H. Sweeney, L.B. Connally, and M.A. Fingerhut. 2001. Spontaneous abortion, sex ratio, and paternal occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Environmental Health Perspectives* 109:1127-32.

72. Mocarelli, P., P. Brambilla, P.M. Gerthoux, D.G. Patterson, Jr., and L.L. Needham. 1996. Change in sex ratio with exposure to dioxin. *Lancet* 348: 409.

73. Moshammer, H., and M. Neuberger. 2000. Sex ratio in the children of the Austrian chloracne cohort. *Lancet* 356:1271-2.

74. Wolfe, W.H., J.E. Michalek, J.C. Miner, A.J. Rahe, C.A. Moore, L.L. Needham, and D.G. Patterson, Jr. 1995. Paternal serum dioxin and reproductive outcomes among veterans of Operation Ranch Hand. *Epidemiology* 6:17-22.

75. Suskind, R.R., and V.S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *The Journal of the American Medical Association* 251:2372-80.

76. Institute of Medicine. 1997. Veterans and Agent Orange: Update 1996. National Academy Press: Washington, DC.

77. Roegner, R.H., W.D. Grubbs, M.B. Lustik, A.S. Brockman, S.C. Henderson, D.E. Williams, W.H. Wolfe, J.E. Michalek, and J.C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

78. American Diabetes Association. 2001. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 24 (Suppl. 1):S5-S20.

79. Garrow, J.S., and J. Webster. 1985. Quetelet's index (W/H^2) as a measure of fatness. *International Journal of Obesity* 9:147-53.

80. Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L. R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

81. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57:369-78.

82. American Diabetes Association. 2003. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care* 26(11):3160-7.

83. Mokdad, A.H., E.S. Ford, B.A. Bowman, W.H. Dietz, F. Vinicor, V.S. Bales, and J.S. Marks. 2003. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. *The Journal of the American Medical Association* 289(1):76-9.

84. Feldman, H.A., C. Longcope, C.A. Derby, C.B. Johannes, A.B. Araujo, A.D. Coviello, W.J. Bremner, and J.B. McKinlay. 2002. Age trends in the level of serum testosterone and other hormones in middle-aged men: Longitudinal results from the Massachusetts Male Aging Study. *Journal of Clinical Endocrinology and Metabolism* 87(2):589-98.

85. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. 2001. Executive Summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *The Journal of the American Medical Association* 285(19):2486-97.

Table of Contents

19 IMMUNOLOGY ASSESSMENT

19.1 INTRODUCTION

19.1.1 Background

19.1.1.1   Organs/Disease

The immune system includes major organs and tissues such as the thymus, spleen, skin, lymphatic system, and bone marrow, as well as cellular components such as white blood cells (WBCs), antibodies, the complement system, and hormone-like substances called cytokines. All WBCs are leukocytes, which arise from the stem cells of the bone marrow. Leukocytes are further subdivided into granulocytes, lymphocytes, and monocytes. Lymphocytes that mature in bone marrow are called B cells, while lymphocytes that mature in the thymus are called T cells. When stimulated, B cells mature into plasma cells, the cells that produce antibodies. Antibodies, or immunoglobulins, fall into one of five classes: IgA, IgD, IgE, IgG, and IgM. Complement refers to serum proteins that are released sequentially in response to infection (the "complement cascade"). Finally, cytokines include lymphokines, interleukins, interferon, and tumor necrosis factor.

T cells are divided into various sets and subsets, defined by cell surface markers that react with monoclonal antibodies that are grouped according to clusters of differentiation (CD) (1). To some extent, CD groupings describe cell function as well. For example, T cells that express CD3 and CD4 surface molecules describe helper T cells, while T cells that express CD3 and CD8 surface molecules are suppressor T cells (1).

There are two types of adaptive immunity responses: humoral immunity, or the production of circulating antibodies in response to an antigen and mediated by B lymphocytes, and cell-mediated immunity, the production of cytotoxic T cells, activated macrophages, activated natural killer cells, and cytokines in response to an antigen.

Ranch Hand and Comparison veterans were evaluated for immunologic function using cell surface marker studies, absolute lymphocytes, quantitative immunoglobulins, and a lupus panel. The lupus panel detects autoantibodies for various autoimmune disorders, such as systemic lupus erythematosus, rheumatoid arthritis, autoimmune thyroiditis, and autoimmune liver diseases, including chronic active hepatitis and primary biliary cirrhosis.

19.1.1.2   Toxicology

Since the early 1970s, when 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin) was shown to cause marked involution of the thymus gland in experimental animals, the immune system has been recognized as a sensitive target of dioxin exposure (2-5). Numerous animal studies have demonstrated that exposure to dioxin increases host susceptibility to a broad range of bacterial (6-11), parasitic (12), and viral (13-16) infectious agents. The extensive body of literature pertinent to dioxin-induced immunotoxicity has been summarized in several review articles (17-23).

Toxic effects of dioxin exposure in laboratory animals have been demonstrated on all components of the immune system, including direct thymotoxic effects, particularly on the epithelial cells (19, 24-27); compromised cell mediated (2, 26, 28-31) and humoral (2, 6, 30, 32-36) immune function; impaired

myeloproliferative (7, 37-40) and lymphoproliferative (26, 38-40) responses; and suppressed complement activity (8, 41-43).

The role of the aryl hydrocarbon (Ah) receptor as a mediator in dioxin toxicity has been long recognized (44, 45) and summarized in several literature reviews (23, 46-48). Much of the basic research in laboratory animals has focused on the role of the Ah receptor in dioxin-induced immunotoxicity, including suppressed humoral (32, 34, 49-55) and cellular (55-58) responses and impaired complement activity in mice (59), but not guinea pigs (60). Other studies demonstrated that dioxin exposure can cause immune system responses independent of the Ah receptor (50, 51, 53, 61-63). Primate experiments of the effects of dioxin on peripheral lymphocyte subpopulations in marmoset (63-67) and rhesus (68) monkeys found the ratios of selected lymphocyte subsets varied inconsistently in response to the dose (high versus low) and duration (acute versus chronic) of exposure. In none of the in vivo studies did the animals demonstrate any overt illness. The Ah receptor has been identified in several human tissues (46, 69-71), and research continues regarding the relevance of these observations to dioxin toxicity in humans.

The demonstration that human tonsils contain the Ah receptor (70) and the development of a tonsillar lymphocyte culture model have established a scientifically valid basis for comparison of the effects of dioxin on experimental animals and humans at the cellular level. In published results from two series of experiments, dioxin had identical effects on both human and murine B lymphocytes with dose-dependent suppression of cellular proliferation and a significant reduction in the secretion of immunoglobulins IgM and IgG (72, 73). Although the mechanism of action is unknown, these experiments provide evidence that the human lymphocyte is sensitive to dioxin, and are consistent with results from another laboratory investigating the effect of dioxin on human lymphocytes isolated from peripheral blood (74). These experimental models have been applied to human populations exposed to dioxin (75, 76).

19.1.1.3   *Epidemiology*

Indicators of immune function have been included in epidemiologic studies of populations exposed to dioxin as a result of environmental contamination (77-86), industrial accidents (87-96), occupational exposure (75, 76, 97-105), and military service in Vietnam (106-113).

Several studies have been conducted that included immunological measures of Missouri residents exposed to dioxin, although there was no evidence for clinical illness among those exposed. Reports of Quail Run, Missouri, residents of a mobile home park with dioxin levels up to 2,200 parts per billion in the soil documented abnormalities in several indices of immune function, including reduced delayed-type hypersensitivity to skin test antigens; significantly lower percentages of CD3, CD4, and CD2 cells; and nonsignificantly decreased CD4 to CD8 ratios in dioxin-exposed persons (77-79). Follow-up examinations found no significant differences in response to delayed-type hypersensitivity skin tests between the exposed and control cohorts, but the mean CD4 to CD8 ratios remained lower in the exposed group (80). No dioxin measurements were made in the exposed populations.

Webb and colleagues conducted a pilot study of health effects associated with dioxin among residents living in the Times Beach, Missouri, area and found no significant differences between high risk and low risk groups in delayed hypersensitivity skin test response, lymphocyte proliferation response, or in a comparison of T-cell subsets (84). A nonsignificant decrease in CD4 to CD8 ratios was seen among high-risk individuals. Follow-up studies measured dioxin levels in adipose tissue among a subset of the high risk group and found significant increases in several immunological indicators associated with dioxin levels in adipose tissue, as well as nonsignificant increases in serum IgA (84, 85).

In a 2002 study of residents of Seveso, Italy, who were exposed to high levels of dioxin from an industrial accident, plasma IgG levels decreased significantly with increasing dioxin plasma concentration (94). No consistent association was seen between dioxin levels and IgM, IgA, and C3 and C4 complement plasma levels. Reports published after the 1976 chemical explosion found no immune system abnormalities in exposed children (87, 88) or cleanup workers (90). Other investigators documented abnormal immune indices in children with chloracne (89, 91) that resolved with time and were not associated with any clinical immune deficiency illness (92, 93). The antinuclear antibody (ANA), immune complexes, and the number of natural killer cells (monoclonal antibody Leu-7) were significantly increased in a cohort of chemical workers exposed to dioxin in an industrial accident in England in 1968 (96); however, these abnormalities were not associated with any clinical illness (95, 96).

Epidemiologic studies have reported results of clinical examinations of workers who experienced significant occupational exposure to dioxin during employment at chemical factories in Germany (75, 76, 97-103) and the United States (104). The studies incorporated immune system parameters in the examination protocols and included serum dioxin data in the analyses, except for one study using insurance claims data that showed an increase in infectious and parasitic diseases among a subgroup of employees with severe chloracne (97). Ott and colleagues reported positive associations between dioxin and increases in IgA and IgG concentrations, marginal increases in complement, and slight decreases in the percentage of lymphocytes (99). Halperin and colleagues found decreased circulating activated T cells and decreased spontaneous proliferation of cultured lymphocytes with higher levels of dioxin (104). None of these studies of occupationally exposed workers showed any evidence of clinical illness associated with immune system disorders among the exposed or any gross abnormalities in the laboratory indices in relation to the body burden of dioxin. In addition, a study of 96 municipal solid waste incinerator workers in Japan did not find an association between serum dioxin levels and immunological function tests (105).

Finally, multiple immunologic indices were examined in relation to serum dioxin levels among members of Operation Ranch Hand veterans (109-112). Michalek and colleagues found no significant associations between dioxin category and mean serum IgA, IgG, or IgM levels, and the percentage of veterans who had an abnormal skin test response was increased in the background and low dioxin category but decreased in the high category (112). Mean absolute total lymphocyte counts and mean absolute lymphocyte subset counts were higher among veterans in the background dioxin category than those in the Comparison category, but no clear patterns were seen between veterans in the low and high dioxin categories. No consistent relations were seen between dioxin exposure and prevalence of the ANA, smooth muscle autoantibodies, mitochondrial autoantibodies, parietal cell autoantibodies, rheumatoid factor, and monoclonal immunoglobulins (112). In a study of 51 Korean Vietnam veterans and 36 nonveterans, total serum IgG levels were significantly decreased and Interleukin 4 (IL-4) levels were significantly increased in veterans exposed to Agent Orange (113).

In 2002, the Institute of Medicine found that the evidence determining whether an association exists between Agent Orange and other herbicides used in Vietnam and immune suppression or autoimmunity was inadequate or insufficient (114).

19.1.2 Summary of Previous Analyses of the Air Force Health Study

19.1.2.1 1982 Baseline Examination Summary Results

Immunologic function and phenotypic marker studies were performed on 592 participants (297 Ranch Hands, 295 Comparisons) randomly selected by the last digit of their participant study identification

number. Because of laboratory problems (e.g., fluctuating quality control and lack of simultaneous differential counts on the peripheral mononuclear cells), data could be analyzed on a group basis only.

Analyses of the cell surface markers (CD2+ or T_{11} [T cells], CD3+ or T_3 [T cells], CD4+ or T_4 [helper T cells], CD8+ or T_8 [suppressor T cells], CD20+ [B cells], the CD4–CD8 [or T_4-T_8] ratio) and the total lymphocyte count (TLC) showed no significant group differences.

Functional studies of T and B cells via reaction to antigenic (tetanus toxoid) or mitogen (phytohemagglutinin [PHA], concanavalin A, and pokeweed) stimulation showed no group differences. Similarly, adjusted mean values of the four assays were not significantly different between groups.

In summary, neither immunologic function nor cell marker studies showed significant impairment in the Ranch Hand group, nor did they show patterns supportive of a herbicide effect.

19.1.2.2   1985 Follow-up Examination Summary Results

The 1985 AFHS physical examination placed more emphasis on the immunology assessment than did the 1982 baseline examination profile. Immunologic competence was measured by cell surface marker (phenotypic) studies and cell stimulation studies on 47 percent of the study population, and by a series of four skin test antigens in 76 percent of the participants to assess the delayed hypersensitivity response.

Surface marker studies were conducted for CD2+ cells (T cells), CD4+ cells (T cells), CD8+ cells (suppressor T cells), CD20+ (B cells), CD14+ cells (monocytes), and human leukocyte antigen-DR (HLA-DR) cells. The ratio of CD4 to CD8 cells also was included in the analysis. Because of inherent significant day-to-day and batch-to-batch variation, all results (including functional stimulation studies) were adjusted for blood-draw day. Statistical testing of the seven phenotypic cell markers did not reveal any significant group differences after adjusting for the covariates of age, race, occupation, current smoking, lifetime smoking history, current alcohol use, or lifetime alcohol use. Similarly, none of the adjusted analyses of the functional stimulation studies (for PHA, pokeweed mitogen, or mixed lymphocyte culture [MLC]) showed any statistically significant group differences. Overall, no pattern was identified to suggest an adverse health effect in any subgroup of either the Ranch Hands or Comparisons.

The delayed hypersensitivity response was assessed by the skin test antigens of mumps, *Candida albicans*, Trichophyton, and staphage lysate. The 48-hour measurements of skin induration and erythema for the four tests showed marked inter-reader variation. Consequently, all skin test data were declared invalid and were not used in the assessment of group differences. The skin test reading problems led to the use of additional clinical quality control procedures for the 1987 follow-up examination.

In conclusion, no significant group differences were found for the comprehensive cell surface marker or functional stimulation studies.

19.1.2.3   1987 Follow-up Examination Summary Results

For the assessment of the 1987 immunologic examination data, results from a composite skin reaction test were evaluated. Various laboratory examination measurements from cell surface marker studies, three groups of functional stimulation tests, and quantitative immunoglobulins also were analyzed. Ranch Hands had a higher frequency of individuals with possibly abnormal reactions on skin testing than Comparisons. For the adjusted analyses of the natural killer assay measurements with and without

Interleukin 2 (IL-2), significant interactions between group and race were present. The clinical meaning of these findings was not apparent and did not point to any known clinical endpoints.

19.1.2.4   Serum Dioxin Analysis of 1987 Follow-up Examination Summary Results

In general, the composite skin test diagnosis results were not associated with serum dioxin levels. The Ranch Hand analyses using initial dioxin and the analyses using dioxin and time since duty in Southeast Asia (SEA) generally displayed nonsignificant decreased risks. For the analyses contrasting Ranch Hands with unknown (termed as "background" in subsequent reports), low, and high dioxin to Comparisons with background dioxin levels, the risks were increased but nonsignificant.

For the most part, the cell surface marker variables and TLC did not display significant associations with serum dioxin. The longitudinal analyses of the CD4-CD8 ratio did not consistently show significant differences in the 1987 ratio relative to the 1985 measurement of the ratio.

For the analyses of PHA net responses, significant positive associations with initial dioxin were found. For the analyses involving dioxin and time since duty in SEA, the maximum PHA net response also displayed some significant positive associations. Depressed immune function would be expected to demonstrate lower PHA net response.

For unstimulated MLC and MLC net response, the three statistical analysis approaches generally displayed nonsignificant associations with serum dioxin. For the analysis involving Ranch Hands in the high dioxin category and Comparisons in the background dioxin category, Ranch Hands had a significantly higher unstimulated MLC mean. The analyses of the natural killer cell variables generally were nonsignificant.

Significant positive associations generally were found between IgA and initial dioxin. The analyses for IgA, IgG, and IgM using dioxin and time since duty in SEA were, for the most part, nonsignificant. For the three immunoglobulins, the overall contrasts of Ranch Hands in the unknown, low, and high dioxin categories versus Comparisons in the background dioxin category generally were significant. For IgA and IgG, the contrasts of Ranch Hands in the unknown dioxin category versus Comparisons in the background dioxin category were significant with Ranch Hands having lower immunoglobulin averages. Ranch Hands in the high dioxin category were not significantly different from Comparisons.

The indices of immune responses analyzed in the 1987 examination provided a comprehensive reflection of in vivo and in vitro immune function in the study population. No clinically meaningful indicators reflecting a relation between the body burden of dioxin or the extrapolated initial exposure and immune function were found. Increased IgA levels may have represented a chronic inflammatory response to dioxin exposure. Elevated erythrocyte sedimentation rates and increased WBC and platelet counts were other examples of indicators that may have represented a chronic inflammatory response to dioxin exposure.

19.1.2.5   1992 Follow-up Examination Summary Results

In general, the composite skin test diagnosis results did not differ significantly between Ranch Hands and Comparisons and were not positively associated with initial or 1987 dioxin levels. For the most part, the cell surface marker variables and total lymphocyte count did not display significant associations with serum dioxin. The longitudinal analyses of the CD4-CD8 ratio did not show significant differences between the 1992 ratio relative to the 1985 measurement of the ratio.

The prevalence of some lupus panel antibodies, such as the mouse stomach kidney (MSK) anti-smooth muscle antibody and the rheumatoid factor, decreased as dioxin exposure increased. This finding was inconsistent with a harmful effect from dioxin. The presence of lupus panel antibodies generally was considered abnormal. A smaller prevalence of the lupus panel antibodies was found in this study than would be expected in the general population. The presence of a smaller prevalence of abnormalities than expected also may have been regarded as an abnormal finding, suggesting a possible early immune alteration.

19.1.2.6   1997 Follow-up Examination Summary Results

The immunology assessment was based on laboratory data on six lymphocyte cell surface markers, absolute lymphocyte counts, three quantitative immunoglobulins, and six measurements from an autoantibody panel. The six cell marker measurements were carried out on a random sample of approximately 40 percent of the participants because of the complexity of the assay and the expense of the tests.

Group analyses revealed significant findings for the adjusted analyses of CD16+56+ cell (natural killer cell) count and for the MSK anti-smooth muscle antibody test in enlisted flyers. Among enlisted flyers, the mean CD16+56+ cell count was greater for Comparisons than for Ranch Hands, and a greater percentage of Comparisons than Ranch Hands had the anti-smooth muscle antibody present. For these analyses the magnitude of the mean differences was small; therefore, the clinical importance of these findings is unknown.

Consistent with the previous two physical examinations, the mean serum concentration of IgA increased significantly with initial dioxin, but was not significantly increased in enlisted groundcrew or the high dioxin category; IgA did not increase significantly with 1987 dioxin. The IgA results, although significant, were small in magnitude and their clinical significance is unknown.

When comparing categorized dioxin levels between Ranch Hands and Comparisons, a significantly higher CD16+56+ cell count mean was observed among Comparisons than among Ranch Hands in the high dioxin category. Analyses revealed significant associations between 1987 dioxin levels and CD3+ cell (T cell) count, CD4+ cell (helper T cell) count, and CD3+CD4+ cell (helper T cell) count. The cell counts increased as 1987 dioxin increased.

In summary, these findings do not provide evidence of a biologically meaningful relation between body burden of dioxin and parameters of immunology assessment.

19.1.3 Parameters for the 2002 Immunology Assessment

19.1.3.1   Dependent Variables

Table 19-1 presents the immunologic measurements that were evaluated and describes their medical importance. The absolute lymphocyte, immunoglobulin studies, and lupus panel tests were conducted on all participants, whereas the cell surface marker studies were carried out on a random sample of approximately 40 percent of the participants because of the complexity of the assay and the expense of the tests.

Table 19-1. Medical Significance of the Immunologic Data

Immunologic Measurements	Rationale of the Measurement	Disease/Syndrome/Condition Endpoint
Cell Surface Marker Studies		
CD3+	Pan-T cell marker (similar to CD2 in previous AFHS examinations). Measures all mature T cells (includes CD4, CD8, etc.). Generally 70 percent or more of peripheral blood lymphocytes are CD3 positive.	Decrease in absolute number of T cells indicates immunodeficiency. May occur because of direct effects of malignancy (e.g., lymphoma), acquired immune deficiency syndrome (AIDS), or chemotherapy. Increase may occur in lymphoproliferative disorders or in some infections.
CD4+	Measures T cells that exhibit helper or inducer phenotype. CD4+ cells initiate an immune response to processed antigens.	Markedly decreased in people with AIDS because of human immunodeficiency virus (HIV) infection of CD4+ cells; increased in autoimmune diseases.
CD8+	Measures T cells that exhibit suppressor and cytotoxic functions. Responsible for appropriate down regulation of an immune response after antigen has been cleared.	Variable in autoimmune diseases; increased in some viral illnesses and immunodeficiencies.
CD20+ (B1)	Measures peripheral blood B cells; no reaction with T cells, granulocytes, or monocytes.	Decreased result in humoral immune deficiency with impaired production of antibodies; increased in lymphoproliferative disorders.
Double-Labeled Cells (cells that express both markers)		
CD3+CD4+	Helper T cells and excludes monocytes but more specific than CD4+.	Same as CD4+.
CD16+56+ (CD3-)	Normally these markers do not occur on the same cells. Measures natural killer cells that can lyse foreign cells independent of antibody or prior contact with the target. CD16+ is an IgG receptor that appears on natural killer cells and neutrophils; CD56+ is more restricted to natural killer cells; joint use of CD16+ and CD56+ enhances enumeration of natural killer cells.	Natural killer cells are thought to attack neoplasms and naturally prevent growth of cancers.
Absolute Lymphocytes		
	Measures absolute number of total lymphocytes circulating in peripheral blood. Major immune mechanism against fungi and viruses.	Decreased in immunodeficiency; increased in lymphoproliferative disorders.

Table 19-1. Medical Significance of the Immunologic Data (Continued)

Immunologic Measurements	Rationale of the Measurement	Disease/Syndrome/Condition Endpoint
Immunoglobulins		
IgG IgA IgM	Each measures ability of specific B cell subgroup to secrete specific antibody class of molecules. Antibodies normally rise in response to infections or immunizations with bacteria, fungi, and viruses. Major immune mechanism against bacteria.	Increased in hyperglobulinemia or myeloma (monoclonal). Decreased in selective or total B cell immunodeficiency. Polyclonal increases in chronic inflammation and liver disease (cirrhosis).
Lupus Panel		
	The test composition of this profile was chosen to include the most frequently encountered autoantibodies. Presence of autoantibodies may indicate specific autoimmune diseases, especially if multiple autoantibodies are present. The individually named autoantibodies (excluding ANA and B cell clones) are associated with specific diseases. Any of these tests may also turn positive as a participant's immune system ages or otherwise is dysregulated.	
ANA Test	Screening assay (performed with monolayers of HEp-2) for many clinically meaningful autoantibodies that occur in systemic rheumatologic diseases.	Positive result suggests possible rheumatologic disease; likelihood increases with number of different positive autoantibodies.
Thyroid Microsomal Antibody	Measures autoantibodies against thyroid microsomal antigen.	Present in autoimmune thyroiditis.
MSK Anti-smooth Muscle Antibody	MSK indicates the tissues used in the assay (mouse stomach kidney); measures autoantibodies against actin in smooth muscle.	Present in autoimmune liver diseases, especially chronic active hepatitis.
MSK Anti-mitochondrial Antibody	Measures autoantibodies against mitochondrial antigens.	Present in autoimmune liver diseases, especially primary biliary cirrhosis.
MSK Anti-parietal Cell Antibody	Measures autoantibodies against parietal cells of the stomach that make intrinsic factor for the absorption of vitamin B_{12}.	Present in pernicious anemia (failure to absorb vitamin B_{12}).
Rheumatoid Factor	Autoantibodies reactive with a person's own antibodies.	Present in rheumatoid arthritis; also in some infections, chronic pulmonary diseases, and other inflammatory or autoimmune diseases.

19.1.3.1.1 Laboratory Variables

The results of cell surface marker studies, absolute lymphocytes, quantitative immunoglobulins, and a lupus panel were analyzed. Participants who were taking anti-inflammatory medication (except aspirin and nonsteroidal) or immunosuppressive medication at the time of the 2002 physical examination were excluded from analysis. Participants who had received x-ray treatment or chemotherapy for cancer within 6 months of the 2002 physical examination and participants who tested positive for HIV also were excluded from analysis.

19.1.3.1.1.1   Cell Surface Marker (Phenotypic) Studies

Quantification of the different cell populations was carried out with the use of reagent mouse monoclonal antibodies using Becton Dickson FACScan equipment. Cell surface markers were analyzed in the statistical evaluation of the immunologic system. The unit of measurement was cells/mm^3.

19.1.3.1.1.2   Absolute Lymphocytes

Absolute lymphocytes indicate the density of lymphocytes in the blood. Lymphocytes recognize and destroy bacteria, fungi, viruses, and other foreign bodies. Statistical analyses were performed on absolute lymphocytes, measured in cells/mm^3 using Becton Dickson FACScan equipment. Absolute lymphocytes also were analyzed in the hematology assessment (see Chapter 16).

19.1.3.1.1.3   Immunoglobulins

Immunoglobulins measure the ability of a specific B-cell subgroup to secrete a specific antibody class of molecules. The antibodies typically rise in response to infections or immunizations with bacteria, fungi, and viruses. Statistical analyses were performed on the immunoglobulins IgA, IgG, and IgM, measured in mg/dL using the Beckman Coulter IMMAGE® system.

19.1.3.1.1.4   Lupus Panel

This group of laboratory tests detected the most frequent autoantibodies found in both patients and asymptomatic individuals. Autoantibodies are markers for autoimmune diseases, and the lupus panel is considered a screening assay for a wide spectrum of autoimmune disorders (e.g., rheumatoid arthritis, systemic lupus erythematosus). Occasionally, autoantibodies are detected in asymptomatic persons; this is alternatively explained as evidence for incipient autoimmune disease or a finding of unknown meaning. In any instance, the finding of an autoantibody is not normal and should be interpreted as an aberration of the immune system. The lupus panel comprises the following individual tests on serum, using a manual indirect fluorescent antibody method:

- ANA performed on HEp-2 cells

- Thyroid microsomal antibody

- MSK section stain for the following specific autoantibodies:

    - Anti-smooth muscle

    - Anti-mitochondrial

    - Anti-parietal cell

- Rheumatoid factor.

All the autoantibodies derive from abnormalities of the B-cell portion, the part of the immune system that produces immunoglobulins.

Statistical analyses were performed on the ANA, thyroid microsomal antibody, MSK anti-smooth muscle antibody, MSK anti-mitochondrial antibody, MSK anti-parietal cell antibody, and rheumatoid factor, with the responses to these tests scored as present or absent.

19.1.3.2 *Covariates*

Covariates used in the immunologic evaluation for adjusted statistical analyses included age, race, military occupation, body mass index (kg/m^2), current cigarette smoking (cigarettes/day), lifetime cigarette smoking history (pack-years), current alcohol use (drinks/day), lifetime alcohol history (drink-years), and a physical activity index (an index combining both duration and intensity of exercise).

Age, race, and military occupation were determined from military records. Body mass index was calculated as weight/(height)^2, where the weight was measured in kilograms and the height was measured in meters at the physical examination (115). For purposes of covariate associations for discrete dependent variables, the body mass index was dichotomized as "not obese" ($\leq$30 kg/m^2) and "obese" (>30 kg/m^2).

Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 2002 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year.

Lifetime alcohol history was based on information from the 2002 questionnaire and combined with similar information gathered at the 1987, 1992, and 1997 follow-up examinations. Each participant was asked about his drinking patterns throughout his lifetime. When a participant's drinking pattern changed, he was asked to describe how his alcohol consumption differed and the duration of time that the drinking pattern lasted. The participant's average daily alcohol consumption was determined for each of the reported drinking pattern periods throughout his lifetime, and an estimate of the corresponding total number of drink-years was derived. One drink-year was the equivalent of drinking 1.5 ounces of an 80-proof alcoholic beverage, one 12-ounce beer, or one 5-ounce glass of wine per day for 1 year. Current alcohol use was defined as the average number of drinks per day during the 2 weeks prior to completing the physical examination.

A series of questions concerning exercise patterns in the 2 weeks prior to the physical examination were included as part of the 2002 questionnaire. The participants were asked questions on frequency, average duration per frequency, and increase of heart rate or breathing for more than 20 different activities. The answers to these questions were used and combined to determine an index of physical activity incorporating duration and intensity (116, 117); this covariate was used in adjusted statistical analyses. A participant was classified as active, moderately active, or sedentary based on his responses to the series of questions regarding exercise patterns.

19.1.4 Statistical Methods

Table 19-2 summarizes the statistical analysis performed for the 2002 immunology assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, exclusions, and statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 19-2.

Table 19-2. Statistical Analysis for the Immunology Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Normal Range/ Cutpoints[a]	Covariates[b]	Exclusions[c]	Statistical Analysis and Methods
CD3+ Cells (T Cells) (cells/mm^3)	LAB	C	700–2,400	(1)	(a)	U:GLM,TT A:GLM
CD4+ Cells (Helper T Cells) (cells/mm^3)	LAB	C	400–1,400	(1)	(a)	U:GLM,TT A:GLM
CD8+ Cells (Suppressor Cells) (cells/mm^3)	LAB	C	300–900	(1)	(a)	U:GLM,TT A:GLM
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)	LAB	C	22–1,200	(1)	(a)	U:GLM,TT A:GLM
CD20+ Cells (B Cells) (cells/mm^3)	LAB	C	33–864	(1)	(a)	U:GLM,TT A:GLM
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)	LAB	C	400–1,400	(1)	(a)	U:GLM,TT A:GLM
Absolute Lymphocytes (cells/mm^3)	LAB	C	1,100–4,800	(1)	(a)	U:GLM,TT A:GLM
IgA (mg/dL)	LAB	C	82–453	(1)	(a)	U:GLM,TT A:GLM
IgG (mg/dL)	LAB	C	751–1,560	(1)	(a)	U:GLM,TT A:GLM
IgM (mg/dL)	LAB	C	46-304	(1)	(a)	U:GLM,TT A:GLM
Lupus Panel: ANA Test	LAB	D	Present Absent	(1)	(a)	U:LR,CS A:LR
Lupus Panel: Thyroid Microsomal Antibody	LAB	D	Present Absent	(1)	(a)	U:LR,CS A:LR
Lupus Panel: MSK Anti-smooth Muscle Antibody	LAB	D	Present Absent	(1)	(a)	U:LR,CS A:LR
Lupus Panel: MSK Anti-mitochondrial Antibody	LAB	D	Present Absent	(1)	(a)	U:LR,CS A:LR

Variable (Units)	Data Source	Data Form	Normal Range/ Cutpoints[a]	Covariates[b]	Exclusions[c]	Statistical Analysis and Methods
Lupus Panel: MSK Anti-parietal Cell Antibody	LAB	D	Present Absent	(1)	(a)	U:LR,CS A:LR
Lupus Panel: Rheumatoid Factor	LAB	D	Present Absent	(1)	(a)	U:LR,CS A:LR

[a]Normal ranges were presented for cell surface markers, absolute lymphocytes, and immunoglobulins for reference purposes. Statistical analyses were done only on the continuous form of these dependent variables.

[b]Covariates:

(1) age, race, military occupation, body mass index, current cigarette smoking, lifetime cigarette smoking history, current alcohol use, lifetime alcohol history, physical activity index.

[c]Exclusions:

(a) participants taking anti-inflammatory (except aspirin and nonsteroidal) or immunosuppressive medications, participants who had received x-ray treatment or chemotherapy for cancer within 6 months of the 2002 physical examination, participants testing positive for HIV.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	C/D	Born $\geq$ 1942 Born < 1942
Race	MIL	D	Black Non-Black
Military Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Body Mass Index (kg/m^2)	PE	C/D	Not Obese: $\leq$30 Obese: >30
Current Cigarette Smoking (cigarettes/day)	Q-SR	C/D	Never Former >0–20 >20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	C/D	0 >0–10 >10
Current Alcohol Use (2 weeks prior to physical exam) (drinks/day)	Q-SR	C/D	0–1 >1
Lifetime Alcohol History (drink-years)	Q-SR	C/D	0 >0–40 >40
Physical Activity Index (kcal/kg/day)	Q-SR	D	Sedentary: <1.45 Moderate: 1.45–<2.95 Very Active: $\geq$2.95

Abbreviations

Data Source:	LAB: 2002 laboratory results
	MIL: Air Force military records
	PE: 2002 physical examination
	Q-SR: Health questionnaires (self-reported)
Data Form:	C: Continuous form of dependent variable
	D: Discrete form of dependent variable or covariate
	C/D: Appropriate form for analysis (either continuous or discrete) of covariate
Statistical Analysis:	U: Unadjusted analysis
	A: Adjusted analysis
Statistical Methods:	CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
	GLM: General linear models analysis
	LR: Logistic regression analysis
	TT: Two-sample t-test

Four models were examined for each dependent variable given in Table 19-2. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for covariates. These covariates are given in Table 19-2. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. In an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-4, the median level of exposure to dioxin was highest for enlisted groundcrew, followed by enlisted flyers, then officers.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the Centers for Disease Control and Prevention (CDC) using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in parts per trillion (ppt) on a lipid weight basis (118). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2. A statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model to account for body mass index-related differences in elimination rate (119).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two

additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. Another category was examined by combining the low and high Ranch Hand categories. This combination is referred to in the tables as the "low plus high Ranch Hand" category. These five categories—Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the four Ranch Hand categories and the dependent variable in the Comparison category was examined. As in Model 2, a statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model for the unadjusted and adjusted analyses of all dependent variables. One Ranch Hand without a dioxin measure was excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The term "unadjusted" was used in the text and tables as follows: Models 1 and 4 did not adjust for any covariates. Models 2 and 3 adjusted only for body mass index at the time of the blood measurement for dioxin. The term "adjusted" was used in the text and tables as follows: Models 1 and 4 adjusted for the covariates shown in Table 19-2 unless otherwise specified by a footnote to the table. Models 2 and 3 additionally adjusted only for body mass index at the time of the blood measurement for dioxin.

Table 19-3 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants that were excluded from analyses is given.

Table 19-3. Number of Participants Excluded or with Missing Data for the Immunology Assessment

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Cell Surface Markers							
CD20+ Cells (B Cells)	DEP	0	1	0	0	0	1
Body Mass Index	COV	0	0	0	0	0	0
Current Cigarette Smoking	COV	0	2	0	0	0	2
Lifetime Cigarette Smoking History	COV	0	3	0	0	0	3
Current Alcohol Use	COV	0	2	0	0	0	2
Lifetime Alcohol History	COV	1	3	1	1	1	3
Physical Activity Index	COV	0	2	0	0	0	2
Taking Anti-inflammatory or Immunosuppressive Medications	EXC	25	30	14	25	25	30

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only) [b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Received X-ray Treatment or Chemotherapy for Cancer Within 6 Months of the 2002 Physical Examination	EXC	6	9	4	6	6	9
Testing Positive for HIV	EXC	0	2	0	0	0	2
Absolute Lymphocytes, Immunoglobulins, and Lupus Panel							
Body Mass Index	COV	1	0	0	1	1	0
Current Cigarette Smoking	COV	0	2	0	0	0	2
Lifetime Cigarette Smoking History	COV	0	3	0	0	0	3
Current Alcohol Use	COV	0	2	0	0	0	2
Lifetime Alcohol History	COV	4	5	3	4	4	5
Physical Activity Index	COV	0	2	0	0	0	2
Taking Anti-inflammatory or Immunosuppressive Medications	EXC	69	88	37	69	69	88
Received X-ray Treatment or Chemotherapy for Cancer Within 6 Months of the 2002 Physical Examination	EXC	12	19	8	12	12	19
Testing Positive for HIV	EXC	3	2	3	3	3	2

Cell Surface Markers:
  [a]302 Ranch Hands and 462 Comparisons for group.
  [b]167 Ranch Hands for initial dioxin; 302 Ranch Hands for 1987 dioxin.
  [c]302 Ranch Hands and 462 Comparisons for categorized dioxin.

Absolute Lymphocytes, Immunoglobulins, and Lupus Panel:
  [a]777 Ranch Hands and 1,174 Comparisons for group.
  [b]424 Ranch Hands for initial dioxin; 776 Ranch Hands for 1987 dioxin.
  [c]776 Ranch Hands and 1,174 Comparisons for categorized dioxin.

Note: COV = Covariate.
         DEP = Dependent variable.
         EXC = Exclusion.

19.2 RESULTS

19.2.1 Dependent Variable-covariate Associations

The complete results of covariate associations with each immunologic dependent variable are documented in Appendix F, Table F-11. These associations were pairwise between the dependent variable and the covariate and were not adjusted for any other covariates. The following paragraphs summarize the pattern of significant (p≤0.05) dependent variable-covariate associations.

Age was significantly associated with absolute lymphocyte count, IgM, ANA, and all cell surface markers except CD8+ cells. CD3+ cells, CD4+ cells, CD20+ cells, CD3+CD4+ cells, absolute lymphocytes, and IgM decreased with increasing age. Natural killer cells (CD16+56+ cells) increased with increasing age. Older participants were more likely to have the ANA present than younger participants.

Blacks had significantly higher CD4+, CD20+, and CD3+CD4+ cell counts than non-Blacks. All three immunoglobulin measures were significantly associated with race. Blacks had higher IgA and IgG levels and lower IgM levels than non-Blacks. Blacks were more likely to have anti-smooth muscle antibodies and less likely to have the ANA present than non-Blacks.

Military occupation was significantly associated with rheumatoid factor, absolute lymphocyte count, IgA, IgG, and all cell surface markers except CD16+56+ cells. Officers had the lowest cell counts (cell surface marker and absolute lymphocyte) and immunoglobulin levels. Except for CD8+ cells, enlisted groundcrew had the highest cell counts and enlisted flyers had the second highest cell counts. For CD8+ cells, enlisted flyers had slightly higher counts than enlisted groundcrew. Rheumatoid factor was more prevalent in enlisted flyers than in enlisted groundcrew or officers.

Body mass index was positively correlated with CD20+ cell and absolute lymphocyte counts. Body mass index was also significantly associated with rheumatoid factor in that obese participants were more likely to have rheumatoid factor present than participants who were not obese.

Current cigarette smoking was significantly associated with the six cell surface markers, absolute lymphocytes, IgG, and rheumatoid factor. As current cigarette smoking increased, all cell surface markers except CD16+56+ cells increased. CD16+56+ cells and IgG levels decreased with increased current smoking. Rheumatoid factor was more prevalent in current smokers than in former smokers or nonsmokers.

Significant increases in CD3+ cells, CD4+ cells, CD8+ cells, CD3+CD4+ cells, and absolute lymphocytes were seen as lifetime cigarette smoking increased. Heavy smokers (more than 10 pack-years) and nonsmokers had the ANA present more often than moderate smokers (less than 10 pack-years). The prevalence of rheumatoid factor increased with increased lifetime cigarette smoking.

Current alcohol use was significantly associated with CD20+ cells, IgG levels, and rheumatoid factor. As current alcohol use increased, CD20+ cell counts and IgG levels decreased. Rheumatoid factor was more prevalent in participants currently drinking more than one drink per day than in participants who drank less.

Significant associations were seen between lifetime alcohol use and CD20+ cells and IgA. CD20+ cell counts decreased with increasing alcohol use and IgA levels increased with increasing alcohol use.

Significant associations were seen between the physical activity index and CD3+ cells, absolute lymphocytes, IgA levels, and thyroid microsomal antibodies. Mean CD3+ cell counts, absolute lymphocyte counts, and IgA levels were higher in sedentary participants than moderately active or very active participants. Thyroid microsomal antibodies were more prevalent in sedentary participants, followed by moderately active participants and very active participants.

19.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 19-2. All dependent variables were obtained from the laboratory measurements during the 2002 physical examination.

19.2.2.1 *Laboratory Variables*

19.2.2.1.1 *CD3+ Cells (T Cells)*

All unadjusted and adjusted analyses of CD3+ cells for Model 1 and Model 2 were nonsignificant (Table 19-4(a-d): p>0.21 for all analyses). The Model 3 unadjusted analyses of CD3+ cells revealed that Ranch Hands in the high dioxin category had a significantly higher mean CD3+ cell count than Comparisons (Table 19-4(e): p=0.036, difference of adjusted means=130.6 cells/mm^3). This contrast was nonsignificant in the Model 3 adjusted analysis (Table 19-4(f): p=0.167). Results from the unadjusted and adjusted analyses of Model 4 were nonsignificant (Table 19-4(g-h): p>0.06 for all analyses).

Table 19-4. Analysis of CD3+ Cells (T Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*272*	*1,234.5*	*31.5*	*0.402*
	Comparison	*422*	*1,203.0*		
Officer	Ranch Hand	119	1,178.5	56.2	0.314
	Comparison	148	1,122.3		
Enlisted Flyer	Ranch Hand	45	1,168.9	-68.0	0.443
	Comparison	78	1,236.9		
Enlisted Groundcrew	Ranch Hand	108	1,329.2	75.5	0.216
	Comparison	196	1,253.8		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 19-4. Analysis of CD3+ Cells (T Cells) (cells/mm³) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*272*	*1,264.3*	*45.1*	*0.231*
	Comparison	*418*	*1,219.1*		
Officer	Ranch Hand	119	1,271.0	68.8	0.242
	Comparison	148	1,202.2		
Enlisted Flyer	Ranch Hand	45	1,215.3	-31.9	0.722
	Comparison	78	1,247.1		
Enlisted Groundcrew	Ranch Hand	108	1,277.7	53.9	0.359
	Comparison	192	1,223.8		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	45	1,192.9	1,193.8	0.008	0.025 (0.027)	0.362
Medium	50	1,316.9	1,315.0			
High	55	1,335.8	1,336.7			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of CD3+ cells (T cells) versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	45	1,223.1	0.135	0.021 (0.032)	0.508
Medium	50	1,318.7			
High	55	1,391.8			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of CD3+ cells (T cells) versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 19-4. Analysis of CD3+ Cells (T Cells) (cells/mm^3) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	422	1,203.0	1,203.0		
Background RH	122	1,175.0	1,174.3	-28.7	0.558
Low RH	72	1,235.2	1,235.5	32.5	0.598
High RH	78	1,332.9	1,333.6	130.6	0.036*
Low plus High RH	150	1,285.1	1,285.6	82.6	0.080

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	418	1,223.1		
Background RH	122	1,225.4	2.3	0.965
Low RH	72	1,290.9	67.8	0.285
High RH	78	1,309.9	86.8	0.167
Low plus High RH	150	1,300.8	77.7	0.102

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 19-4. Analysis of CD3+ Cells (T Cells) (cells/mm^3) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	95	1,127.6	0.013	0.030 (0.016)	0.063
Medium	83	1,266.0			
High	94	1,323.1			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of CD3+ cells (T cells) versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	95	1,064.8	0.081	0.016 (0.020)	0.419
Medium	83	1,222.6			
High	94	1,177.8			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of CD3+ cells (T cells) versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

19.2.2.1.2   CD4+ Cells (Helper T Cells)

The unadjusted and adjusted analyses of CD4+ cells for Model 1 and Model 2 were nonsignificant (Table 19-5(a–d): p>0.25 for all analyses). The unadjusted analyses of Model 3 revealed a significantly higher mean CD4+ cell count for Ranch Hands in the high dioxin category than Comparisons (Table 19-5(e): p=0.036, difference of adjusted means=90.4 cells/mm^3). This contrast was nonsignificant in the Model 3 adjusted analysis (Table 19-5(f): p=0.133). Results from the Model 4 unadjusted analysis and adjusted analyses of CD4+ cells were nonsignificant (Table 19-5(g-h): p>0.06 for all analyses).

Table 19-5. Analysis of CD4+ Cells (Helper T Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*272*	*887.8*	*15.7*	*0.553*
	Comparison	*422*	*872.1*		
Officer	Ranch Hand	119	855.4	30.7	0.453
	Comparison	148	824.8		
Enlisted Flyer	Ranch Hand	45	824.8	-59.4	0.343
	Comparison	78	884.3		
Enlisted Groundcrew	Ranch Hand	108	951.7	47.9	0.252
	Comparison	196	903.8		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*272*	*928.8*	*22.3*	*0.397*
	Comparison	*418*	*906.5*		
Officer	Ranch Hand	119	958.7	40.7	0.330
	Comparison	148	917.9		
Enlisted Flyer	Ranch Hand	45	890.6	-29.2	0.641
	Comparison	78	919.8		
Enlisted Groundcrew	Ranch Hand	108	918.0	25.9	0.522
	Comparison	192	892.1		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Table 19-5. Analysis of CD4+ Cells (Helper T Cells) (cells/mm^3) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

		Initial Dioxin Category Summary Statistics		Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	45	868.3	869.7	0.016	0.354 (0.371)	0.341
Medium	50	951.9	949.1			
High	55	944.9	946.2			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of CD4+ cells (helper T cells) versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

		Initial Dioxin Category Summary Statistics	Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	45	927.7	0.168	0.348 (0.439)	0.429
Medium	50	1,000.3			
High	55	1,014.2			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of CD4+ cells (helper T cells) versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	422	872.1	872.1		
Background RH	122	844.5	843.7	-28.4	0.415
Low RH	72	883.8	884.2	12.1	0.781
High RH	78	961.6	962.5	90.4	0.036*
Low plus High RH	150	923.9	924.5	52.4	0.112

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 19-5. Analysis of CD4+ Cells (Helper T Cells) (cells/mm^3) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	418	910.7		
Background RH	122	892.3	-18.4	0.612
Low RH	72	950.2	39.5	0.369
High RH	78	976.3	65.6	0.133
Low plus High RH	150	963.8	53.1	0.108

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	95	815.5	0.013	0.406 (0.218)	0.063
Medium	83	898.7			
High	94	954.1			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of CD4+ cells (helper T cells) versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	95	816.9	0.089	0.288 (0.272)	0.292
Medium	83	919.8			
High	94	932.7			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of CD4+ cells (helper T cells) versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

19.2.2.1.3   CD8+ Cells (Suppressor T Cells)

All results from the unadjusted and adjusted analyses of CD8+ cells in Models 1 through 4 were nonsignificant (Table 19-6(a–h): p>0.17 for all analyses).

Table 19-6. Analysis of CD8+ Cells (Suppressor T Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*272*	*527.1*	*9.5*	*0.629*
	Comparison	*422*	*517.5*		
Officer	Ranch Hand	119	496.5	10.4	0.722
	Comparison	148	486.1		
Enlisted Flyer	Ranch Hand	45	540.9	-19.9	0.690
	Comparison	78	560.8		
Enlisted Groundcrew	Ranch Hand	108	556.9	31.3	0.318
	Comparison	196	525.6		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*272*	*548.7*	*16.3*	*0.426*
	Comparison	*418*	*532.4*		
Officer	Ranch Hand	119	512.1	9.9	0.742
	Comparison	148	502.2		
Enlisted Flyer	Ranch Hand	45	543.3	-21.1	0.675
	Comparison	78	564.4		
Enlisted Groundcrew	Ranch Hand	108	579.7	38.4	0.242
	Comparison	192	541.3		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 19-6. Analysis of CD8+ Cells (Suppressor T Cells) (cells/mm³) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	45	533.0	533.9	0.010	0.010 (0.027)	0.703
Medium	50	539.5	537.7			
High	55	553.0	553.8			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of CD8+ cells (suppressor T cells) versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	45	531.2	0.029	0.017 (0.035)	0.628
Medium	50	544.2			
High	55	563.8			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of CD8+ cells (suppressor T cells) versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	422	517.5	517.6		
Background RH	122	508.8	508.2	-9.4	0.718
Low RH	72	541.6	541.9	24.3	0.459
High RH	78	543.2	543.7	26.1	0.412
Low plus High RH	150	542.4	542.8	25.2	0.304

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 19-6. Analysis of CD8+ Cells (Suppressor T Cells) (cells/mm³) (Continued)

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	418	532.7		
Background RH	122	544.3	11.6	0.683
Low RH	72	552.0	19.3	0.572
High RH	78	550.8	18.1	0.590
Low plus High RH	150	551.4	18.7	0.463

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
　　　　Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
　　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
　　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	95	480.1	0.007	0.025 (0.019)	0.172
Medium	83	571.3			
High	94	539.4			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of CD8+ cells (suppressor T cells) versus $\log_2$ (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	95	462.0	0.055	0.007 (0.024)	0.769
Medium	83	543.9			
High	94	467.4			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of CD8+ cells (suppressor T cells) versus $\log_2$ (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

19.2.2.1.4 CD16+56+ Cells (Natural Killer Cells)

All results from the unadjusted and adjusted analyses of CD16+56+ cells in Models 1 through 4 were nonsignificant (Table 19-7(a–h): $p>0.20$ for all analyses).

Table 19-7. Analysis of CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*272*	*222.2*	*-1.5*	*0.873*
	Comparison	*422*	*223.7*		
Officer	Ranch Hand	119	215.6	-4.6	0.745
	Comparison	148	220.2		
Enlisted Flyer	Ranch Hand	45	225.4	-15.9	0.493
	Comparison	78	241.2		
Enlisted Groundcrew	Ranch Hand	108	228.4	8.8	0.538
	Comparison	196	219.6		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*272*	*226.4*	*0.7*	*0.938*
	Comparison	*418*	*225.6*		
Officer	Ranch Hand	119	209.7	-4.1	0.763
	Comparison	148	213.8		
Enlisted Flyer	Ranch Hand	45	218.4	-20.6	0.364
	Comparison	78	239.0		
Enlisted Groundcrew	Ranch Hand	108	245.2	15.1	0.320
	Comparison	192	230.1		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 19-7. Analysis of CD16+56+ Cells (Natural Killer Cells) (cells/mm³) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	45	254.8	255.6	0.021	-0.035 (0.035)	0.328
Medium	50	213.5	212.2			
High	55	228.4	229.0			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of CD16+56+ cells (natural killer cells) versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	45	267.4	0.076	-0.055 (0.044)	0.212
Medium	50	207.0			
High	55	213.1			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of CD16+56+ cells (natural killer cells) versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	422	223.7	223.7		
Background RH	122	212.2	213.6	-10.1	0.400
Low RH	72	244.3	243.6	19.9	0.206
High RH	78	218.9	217.5	-6.2	0.672
Low plus High RH	150	230.7	229.7	6.0	0.599

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	418	225.3		
Background RH	122	222.1	-3.2	0.804
Low RH	72	238.2	12.9	0.417
High RH	78	219.7	-5.6	0.712
Low plus High RH	150	228.4	3.1	0.788

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log₂ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	95	210.4	0.003	0.018 (0.021)	0.379
Medium	83	237.0			
High	94	221.9			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of CD16+56+ cells (natural killer cells) versus log₂ (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log₂ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	95	220.8	0.059	-0.009 (0.026)	0.726
Medium	83	236.2			
High	94	207.1			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of CD16+56+ cells (natural killer cells) versus log₂ (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

19.2.2.1.5   CD20+ Cells (B Cells)

All unadjusted and adjusted Model 1 results from the analyses of CD20+ cell count were nonsignificant (Table 19-8(a,b): p>0.37 for all analyses). The Model 2 unadjusted and adjusted analyses revealed a significant positive association between initial dioxin and CD20+ cell count (Table 19-8(c,d): p=0.001, Slope=0.119, unadjusted; p=0.016, Slope=0.102, adjusted). The adjusted means for the low, medium, and high initial dioxin categories were 187.2, 263.8, and 257.7 cells/mm^3, respectively.

The unadjusted analyses of Model 3 revealed that Ranch Hands in the low dioxin category had a significantly lower mean CD20+ cell count than Comparisons (Table 19-8(e): p=0.016, difference of adjusted means=-34.1 cells/mm^3). Ranch Hands in the high dioxin category, however, were found to have a higher mean CD20+ cell count than Comparisons (Table 19-8(e): p=0.047, difference of adjusted means=32.7 cells/mm^3). The Model 3 adjusted analyses did not reveal significant differences (Table 19-8(f): p≥0.09 for all analyses).

The Model 4 unadjusted analysis revealed a positive association between initial dioxin level and CD20+ cell count (Table 19-8(g): p=0.042, Slope=0.046). The association was nonsignificant, however, in the adjusted analysis (Table 19-8(h): p=0.601).

Table 19-8. Analysis of CD20+ Cells (B Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*272*	*181.3*	*-8.1*	*0.388*
	Comparison	*422*	*189.4*		
Officer	Ranch Hand	119	161.4	-5.6	0.666
	Comparison	148	167.0		
Enlisted Flyer	Ranch Hand	45	167.7	-18.9	0.373
	Comparison	78	186.7		
Enlisted Groundcrew	Ranch Hand	108	212.8	3.4	0.834
	Comparison	196	209.4		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 19-8. Analysis of CD20+ Cells (B Cells) (cells/mm³) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*272*	*190.6*	*-6.6*	*0.489*
	Comparison	*418*	*197.1*		
Officer	Ranch Hand	119	187.9	-5.1	0.728
	Comparison	148	193.0		
Enlisted Flyer	Ranch Hand	45	188.5	-12.9	0.573
	Comparison	78	201.4		
Enlisted Groundcrew	Ranch Hand	108	193.0	-5.4	0.716
	Comparison	192	198.4		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	45	142.3	142.9	0.107	0.119 (0.035)	0.001**
Medium	50	214.5	212.7			
High	55	205.6	206.5			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of CD20+ cells (B cells) versus log_2 (initial dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	45	187.2	0.228	0.102 (0.042)	0.016*
Medium	50	263.8			
High	55	257.7			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of CD20+ cells (B cells) versus log_2 (initial dioxin).

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 19-8. Analysis of CD20+ Cells (B Cells) (cells/mm^3) (Continued)

(e) MODEL 3: RANCH HANDS AND COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	422	189.4	189.4		
Background RH	122	174.8	174.4	-15.0	0.219
Low RH	72	155.1	155.3	-34.1	0.016*
High RH	78	221.6	222.1	32.7	0.047*
Low plus High RH	150	186.7	187.0	-2.4	0.839

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	418	198.5		
Background RH	122	191.1	-7.4	0.572
Low RH	72	173.1	-25.4	0.090
High RH	78	209.6	11.1	0.494
Low plus High RH	150	191.2	-7.3	0.534

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 19-8. Analysis of CD20+ Cells (B Cells) (cells/mm^3) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	95	170.3	0.015	0.046 (0.022)	0.042*
Medium	83	164.5			
High	94	210.4			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of CD20+ cells (B cells) versus log$_2$ (1987 dioxin).

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	95	200.7	0.128	0.014 (0.028)	0.601
Medium	83	194.6			
High	94	217.1			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of CD20+ cells (B cells) versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

19.2.2.1.6   CD3+CD4+ Cells (Helper T Cells)

All unadjusted and adjusted analyses of CD3+CD4+ cell count for Models 1, 2 and 4 were nonsignificant (Table 19-9(a-d,g,h): p>0.07 for all analyses). The Model 3 unadjusted analyses of CD3+CD4+ cell count revealed that Ranch Hands in the high dioxin category have a higher mean CD3+CD4+ cell count than Comparisons (Table 19-9(e): p=0.026, difference of adjusted means=92.5 cells/mm^3). The adjusted analysis, however, was nonsignificant for this contrast (Table 19-9(f): p=0.106).

Table 19-9. Analysis of CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*272*	*820.9*	*16.9*	*0.506*
	Comparison	*422*	*804.0*		
Officer	Ranch Hand	119	789.5	31.7	0.419
	Comparison	148	757.9		
Enlisted Flyer	Ranch Hand	45	761.5	-54.3	0.366
	Comparison	78	815.8		
Enlisted Groundcrew	Ranch Hand	108	882.1	47.2	0.239
	Comparison	196	834.9		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*272*	*855.7*	*23.2*	*0.356*
	Comparison	*418*	*832.5*		
Officer	Ranch Hand	119	885.3	41.4	0.299
	Comparison	148	843.9		
Enlisted Flyer	Ranch Hand	45	821.7	-23.6	0.693
	Comparison	78	845.2		
Enlisted Groundcrew	Ranch Hand	108	842.7	25.0	0.517
	Comparison	192	817.7		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Table 19-9. Analysis of CD3+CD4+ Cells (Helper T Cells) (cells/mm³) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

		Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	45	790.4	791.7	0.018	0.409 (0.373)	0.274
Medium	50	884.9	882.2			
High	55	876.4	877.7			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of CD3+CD4+ cells (helper T cells) versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

		Initial Dioxin Category Summary Statistics		Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	45	843.9	0.173	0.350 (0.440)	0.428
Medium	50	918.6			
High	55	930.8			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of CD3+CD4+ cells (helper T cells) versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	422	804.0	804.0		
Background RH	122	782.4	781.4	-22.6	0.500
Low RH	72	807.9	808.4	4.4	0.916
High RH	78	895.5	896.5	92.5	0.026*
Low plus High RH	150	852.9	853.6	49.6	0.116

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented
  because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	418	836.6		
Background RH	122	823.8	-12.8	0.710
Low RH	72	868.9	32.3	0.441
High RH	78	904.1	67.5	0.106
Low plus High RH	150	887.1	50.5	0.108

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	95	756.1	0.012	0.389 (0.218)	0.075
Medium	83	823.7			
High	94	886.5			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of CD3+CD4+ cells (helper T cells) versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	95	749.0	0.092	0.248 (0.272)	0.362
Medium	83	836.6			
High	94	852.2			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of CD3+CD4+ cells (helper T cells) versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

19.2.2.1.7   Absolute Lymphocytes

All unadjusted and adjusted analyses results from Model 1 for absolute lymphocytes were nonsignificant (Table 19-10(a,b): p>0.29 for all analyses). The unadjusted analyses for Models 2 and 4 were significant, revealing positive associations between initial dioxin and absolute lymphocytes (Table 19-10(c): p=0.029, Slope=0.031; and Table 19-10(g): p=0.029, Slope=0.021). The adjusted analyses for Models 2 and 4 were nonsignificant (Table 19-10(d,h): p>0.22 for all adjusted Model 2 and 4 analyses).

The unadjusted analyses of absolute lymphocytes in Model 3 revealed a significantly higher mean absolute lymphocyte count for Ranch Hands in the high dioxin category than Comparisons (Table 19-10(e): p=0.017, difference of adjusted means=129.6 cells/mm^3). The adjusted analyses of Model 3 were nonsignificant (Table 19-10(f): p>0.44 for all analyses).

Table 19-10. Analysis of Absolute Lymphocytes (cells/mm^3)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*695*	*1,665.7*	*13.2*	*0.684*
	Comparison	*1,068*	*1,652.6*		
Officer	Ranch Hand	276	1,538.2	-14.6	0.759
	Comparison	417	1,552.8		
Enlisted Flyer	Ranch Hand	116	1,662.9	-2.8	0.972
	Comparison	167	1,665.6		
Enlisted Groundcrew	Ranch Hand	303	1,792.3	53.3	0.298
	Comparison	484	1,739.0		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*692*	*1,656.8*	*10.7*	*0.735*
	Comparison	*1,064*	*1,646.0*		
Officer	Ranch Hand	275	1,589.7	-9.6	0.843
	Comparison	417	1,599.3		
Enlisted Flyer	Ranch Hand	115	1,652.8	-1.3	0.987
	Comparison	167	1,654.1		
Enlisted Groundcrew	Ranch Hand	302	1,726.4	34.9	0.479
	Comparison	480	1,691.5		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 19-10. Analysis of Absolute Lymphocytes (cells/mm³) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	123	1,616.4	1,614.6	0.013	0.031 (0.014)	0.029*
Medium	128	1,758.4	1,758.7			
High	126	1,763.7	1,765.3			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (initial dioxin).

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	123	1,597.5	0.085	0.021 (0.017)	0.222
Medium	128	1,693.7			
High	125	1,696.4			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute lymphocytes versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 19-10. Analysis of Absolute Lymphocytes (cells/mm³) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,068	1,652.6	1,652.7		
Background RH	317	1,607.6	1,606.9	-45.8	0.276
Low RH	187	1,645.0	1,645.2	-7.5	0.886
High RH	190	1,781.5	1,782.3	129.6	0.017*
Low plus High RH	377	1,712.5	1,712.9	60.2	0.135

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented
  because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant ($0.010 < p\text{-value} \leq 0.050$).

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,064	1,650.6		
Background RH	315	1,643.6	-7.0	0.870
Low RH	187	1,639.2	-11.4	0.825
High RH	189	1,691.7	41.1	0.441
Low plus High RH	376	1,665.4	14.8	0.708

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented
  because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 19-10. Analysis of Absolute Lymphocytes (cells/mm^3) (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	242	1,574.3	0.007	0.021 (0.009)	0.029*
Medium	224	1,643.8			
High	228	1,785.2			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute lymphocytes versus log$_2$ (1987 dioxin).

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	241	1,582.5	0.074	-0.004 (0.011)	0.704
Medium	223	1,628.2			
High	227	1,647.7			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of absolute lymphocytes versus log$_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

19.2.2.1.8 IgA

All unadjusted and adjusted analyses of IgA from Models 1 through 4 were nonsignificant (Table 19-11(a–h): p>0.09 for all analyses).

Table 19-11. Analysis of IgA (mg/dL)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*695*	*254.8*	*-3.5*	*0.549*
	Comparison	*1,068*	*258.3*		
Officer	Ranch Hand	276	247.3	-0.7	0.942
	Comparison	417	248.0		
Enlisted Flyer	Ranch Hand	116	253.6	-6.7	0.648
	Comparison	167	260.2		
Enlisted Groundcrew	Ranch Hand	303	262.1	-4.6	0.612
	Comparison	484	266.7		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS − ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*692*	*267.5*	*-1.1*	*0.859*
	Comparison	*1,064*	*268.6*		
Officer	Ranch Hand	275	255.5	-0.7	0.938
	Comparison	417	256.2		
Enlisted Flyer	Ranch Hand	115	265.2	-4.1	0.786
	Comparison	167	269.3		
Enlisted Groundcrew	Ranch Hand	302	281.1	-0.3	0.975
	Comparison	480	281.4		

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Table 19-11. Analysis of IgA (mg/dL) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	123	259.9	260.6	0.004	0.089 (0.140)	0.526
Medium	128	259.5	259.4			
High	126	264.5	263.8			

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on square root of IgA versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	123	283.7	0.051	0.193 (0.169)	0.256
Medium	128	290.0			
High	125	295.4			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of IgA versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,068	258.3	258.1		
Background RH	317	246.3	248.3	-9.8	0.205
Low RH	187	264.7	264.3	6.2	0.521
High RH	190	257.9	256.0	-2.1	0.830
Low plus High RH	377	261.3	260.1	2.0	0.781

[a]Transformed from square root scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[d]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 19-11. Analysis of IgA (mg/dL) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,064	267.5		
Background RH	315	263.7	-3.8	0.642
Low RH	187	276.1	8.6	0.382
High RH	189	263.3	-4.2	0.675
Low plus High RH	376	269.6	2.1	0.774

[a]Transformed from square root scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on square root scale.
[c]P-value was based on difference of means on square root scale.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	242	242.2	0.004	0.147 (0.088)	0.096
Medium	224	260.2			
High	228	261.8			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of IgA versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	241	264.0	0.034	0.098 (0.105)	0.354
Medium	223	277.7			
High	227	276.8			

[a]Transformed from square root scale.
[b]Slope and standard error based on square root of IgA versus log_2 (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

19.2.2.1.9   IgG

All unadjusted and adjusted analyses of IgG from Models 1, 2 and 4 were nonsignificant (Table 19-11(a-d,g,h): p≥0.13 for all analyses). The unadjusted Model 3 analyses revealed a significantly lower mean IgG level for Ranch Hands in the background dioxin category versus Comparisons (Table 19-12(e): p=0.045, difference of adjusted means=-34.6 cells/mm^3). In the adjusted analyses of Model 3, there were no significant differences (Table 19-12(f): p>0.20 for all analyses).

Table 19-12. Analysis of IgG (mg/dL)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*695*	*1,046.1*	*-19.8*	*0.131*
	Comparison	*1,068*	*1,065.9*		
Officer	Ranch Hand	276	1,010.2	-28.8	0.155
	Comparison	417	1,039.0		
Enlisted Flyer	Ranch Hand	116	1,050.0	-32.1	0.327
	Comparison	167	1,082.2		
Enlisted Groundcrew	Ranch Hand	303	1,078.4	-5.7	0.779
	Comparison	484	1,084.0		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*692*	*1,146.3*	*-17.6*	*0.211*
	Comparison	*1,064*	*1,163.9*		
Officer	Ranch Hand	275	1,105.4	-32.8	0.130
	Comparison	417	1,138.2		
Enlisted Flyer	Ranch Hand	115	1,145.3	-34.6	0.325
	Comparison	167	1,179.9		
Enlisted Groundcrew	Ranch Hand	302	1,183.8	3.1	0.885
	Comparison	480	1,180.7		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Table 19-12. Analysis of IgG (mg/dL) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	123	1,052.2	1,052.2	<0.001	0.001 (0.010)	0.956
Medium	128	1,091.2	1,091.2			
High	126	1,039.3	1,039.4			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of IgG versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	123	1,140.1	0.098	-0.001 (0.012)	0.928
Medium	128	1,179.2			
High	125	1,114.2			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of IgG versus log_2 (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,068	1,065.9	1,065.7		
Background RH	317	1,028.3	1,031.1	-34.6	0.045*
Low RH	187	1,069.2	1,068.6	2.9	0.892
High RH	190	1,052.8	1,050.1	-15.6	0.467
Low plus High RH	377	1,060.9	1,059.3	-6.4	0.694

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 19-12. Analysis of IgG (mg/dL) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,064	1,163.0		
Background RH	315	1,139.0	-24.0	0.204
Low RH	187	1,159.7	-3.3	0.886
High RH	189	1,142.6	-20.4	0.385
Low plus High RH	376	1,151.1	-11.9	0.498

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	242	1,026.3	0.002	0.007 (0.006)	0.275
Medium	224	1,048.0			
High	228	1,064.9			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of IgG versus $\log_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	241	1,131.4	0.063	-0.001 (0.007)	0.885
Medium	223	1,132.2			
High	227	1,139.8			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of IgG versus $\log_2$ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

19.2.2.1.10   IgM

Comparisons were found to have a significantly higher mean IgM level than Ranch Hands within the enlisted flyer stratum for both the Model 1 unadjusted and adjusted analyses (Table 19-13(a): p=0.020, difference of means=-15.54 cells/mm^3, unadjusted; Table 19-13(b): p=0.031, difference of means= -13.82 cells/mm^3, adjusted). The Model 2 through 4 unadjusted and adjusted analyses of IgM were nonsignificant (Table 19-13(c–h): p>0.18 for all analyses).

Table 19-13. Analysis of IgM (mg/dL)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*695*	*89.15*	*-2.25*	*0.403*
	Comparison	*1,068*	*91.40*		
Officer	Ranch Hand	276	85.43	-2.62	0.523
	Comparison	417	88.05		
Enlisted Flyer	Ranch Hand	116	82.99	-15.54	0.020*
	Comparison	167	98.53		
Enlisted Groundcrew	Ranch Hand	303	95.26	3.29	0.431
	Comparison	484	91.97		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*692*	*84.42*	*-1.75*	*0.494*
	Comparison	*1,064*	*86.17*		
Officer	Ranch Hand	275	81.86	-1.78	0.650
	Comparison	417	83.64		
Enlisted Flyer	Ranch Hand	115	80.01	-13.82	0.031*
	Comparison	167	93.83		
Enlisted Groundcrew	Ranch Hand	302	87.52	2.67	0.491
	Comparison	480	84.86		

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

*: Statistically significant (0.010<p-value≤0.050).

Table 19-13. Analysis of IgM (mg/dL) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	123	86.06	85.93	0.001	0.007 (0.023)	0.760
Medium	128	88.72	88.74			
High	126	91.96	92.07			

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of IgM versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	123	75.93	0.066	-0.013 (0.028)	0.634
Medium	128	76.06			
High	125	78.52			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of IgM versus log$_2$ (initial dioxin).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,068	91.40	91.49		
Background RH	317	89.59	88.61	-2.88	0.416
Low RH	187	87.47	87.67	-3.82	0.378
High RH	190	90.34	91.26	-0.23	0.957
Low plus High RH	377	88.90	89.46	-2.03	0.540

[a]Transformed from natural logarithm scale.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[d]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 19-13. Analysis of IgM (mg/dL) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,064	86.34		
Background RH	315	85.85	-0.49	0.887
Low RH	187	83.40	-2.94	0.477
High RH	189	82.77	-3.57	0.396
Low plus High RH	376	83.08	-3.26	0.300

[a]Transformed from natural logarithm scale.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale.
[c]P-value was based on difference of means on natural logarithm scale.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean[a]	R^2	Slope (Standard Error)[b]	p-Value
Low	242	89.67	<0.001	-0.002 (0.014)	0.902
Medium	224	88.28			
High	228	89.66			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of IgM versus $\log_2$ (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (1987 Dioxin)		
1987 Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	241	80.37	0.036	-0.023 (0.017)	0.188
Medium	223	79.05			
High	227	74.32			

[a]Transformed from natural logarithm scale.
[b]Slope and standard error based on natural logarithm of IgM versus $\log_2$ (1987 dioxin).

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

19.2.2.1.11 Lupus Panel: ANA Test

All unadjusted and adjusted analyses results from Models 1, 3, and 4 for the ANA were nonsignificant
(Table 19--14(a,b,e-h): p>0.05). A significant positive association was found between initial dioxin and
the presence of the ANA in both the unadjusted and adjusted analyses of Model 2 (Table 19-14(c,d):
Unadjusted Relative Risk [RR]=1.22, p=0.037; Adjusted RR=1.28, p=0.035, respectively). The
percentages of Ranch Hands with the ANA present were 19.5, 11.7, and 27.8 percent in the low, medium,
and high initial dioxin categories, respectively.

Table 19-14. Analysis of Lupus Panel: ANA Test

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*695*	*133 (19.1)*	*1.00 (0.79,1.28)*	*0.985*
	Comparison	*1,068*	*204 (19.1)*		
Officer	Ranch Hand	276	52 (18.8)	0.87 (0.59,1.27)	0.468
	Comparison	417	88 (21.1)		
Enlisted Flyer	Ranch Hand	116	20 (17.2)	1.03 (0.55,1.94)	0.917
	Comparison	167	28 (16.8)		
Enlisted Groundcrew	Ranch Hand	303	61 (20.1)	1.13 (0.79,1.63)	0.497
	Comparison	484	88 (18.2)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,756*	*0.99 (0.77,1.27)*	*0.946*
Officer	692	0.87 (0.59,1.27)	0.461
Enlisted Flyer	282	1.01 (0.53,1.91)	0.978
Enlisted Groundcrew	782	1.12 (0.77,1.62)	0.548

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	123	24 (19.5)	1.22 (1.01,1.47)	0.037*
Medium	128	15 (11.7)		
High	126	35 (27.8)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 19-14. Analysis of Lupus Panel: ANA Test (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log$_2$ (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
376	1.28 (1.02,1.61)	0.035*

[a]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,068	204 (19.1)		
Background RH	317	59 (18.6)	0.96 (0.70,1.33)	0.829
Low RH	187	31 (16.6)	0.84 (0.56,1.27)	0.416
High RH	190	43 (22.6)	1.24 (0.85,1.81)	0.255
Low plus High RH	377	74 (19.6)	1.02 (0.76,1.38)	0.875

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,064		
Background RH	315	0.92 (0.66,1.29)	0.632
Low RH	187	0.82 (0.54,1.25)	0.364
High RH	189	1.33 (0.90,1.97)	0.153
Low plus High RH	376	1.05 (0.77,1.43)	0.766

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
　　　Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 19-14. Analysis of Lupus Panel: ANA Test (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Present**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	242	40 (16.5)	1.12 (0.99,1.25)	0.067
Medium	224	44 (19.6)		
High	228	49 (21.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
691	1.15 (0.99,1.33)	0.058

[a]Relative risk for a twofold increase in 1987 dioxin.

19.2.2.1.12 Lupus Panel: Thyroid Microsomal Antibody

All results from the unadjusted and adjusted analyses of the thyroid microsomal antibody in Models 1 through 4 were nonsignificant (Table 19-15(a-h): p>0.12 for all analyses).

Table 19-15. Analysis of Lupus Panel: Thyroid Microsomal Antibody

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*695*	*23 (3.3)*	*1.49 (0.83,2.66)*	*0.181*
	Comparison	*1,068*	*24 (2.2)*		
Officer	Ranch Hand	276	9 (3.3)	1.37 (0.55,3.42)	0.498
	Comparison	417	10 (2.4)		
Enlisted Flyer	Ranch Hand	116	2 (1.7)	0.71 (0.13,3.97)	0.701
	Comparison	167	4 (2.4)		
Enlisted Groundcrew	Ranch Hand	303	12 (4.0)	1.95 (0.83,4.58)	0.123
	Comparison	484	10 (2.1)		

Table 19-15. Analysis of Lupus Panel: Thyroid Microsomal Antibody (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,756*	*1.56 (0.86,2.80)*	*0.143*
Officer	692	1.48 (0.59,3.72)	0.407
Enlisted Flyer	282	0.74 (0.13,4.18)	0.736
Enlisted Groundcrew	782	1.97 (0.83,4.68)	0.122

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	123	5 (4.1)	0.99 (0.66,1.51)	0.979
Medium	128	4 (3.1)		
High	126	4 (3.2)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
376	0.84 (0.51,1.38)	0.483

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with a thyroid microsomal antibody present.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,068	24 (2.2)		
Background RH	317	10 (3.2)	1.46 (0.69,3.11)	0.327
Low RH	187	6 (3.2)	1.44 (0.58,3.57)	0.434
High RH	190	7 (3.7)	1.63 (0.69,3.85)	0.267
Low plus High RH	377	13 (3.4)	1.53 (0.77,3.04)	0.226

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,064		
Background RH	315	1.48 (0.67,3.24)	0.329
Low RH	187	1.64 (0.65,4.14)	0.298
High RH	189	1.68 (0.68,4.13)	0.262
Low plus High RH	376	1.66 (0.82,3.36)	0.162

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	242	8 (3.3)	1.02 (0.79,1.32)	0.895
Medium	224	7 (3.1)		
High	228	8 (3.5)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED		
Analysis Results for Log$_2$ (1987 Dioxin)		
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
691	1.01 (0.75,1.37)	0.944

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with a thyroid microsomal antibody present.

19.2.2.1.13   Lupus Panel: MSK Anti-smooth Muscle Antibody

Because of the sparse number of participants with the MSK anti-smooth muscle antibody present (9 Ranch Hands and 8 Comparisons), analysis was limited. The Model 1 unadjusted analysis did not reveal significant findings (Table 19-16(a): p>0.06 for all analyses). The adjusted analysis of Model 1, however, revealed a significant difference in the presence of the MSK anti-smooth muscle antibody between Ranch Hands and Comparisons in the officer stratum (Table 19-16(b): p=0.045, Adjusted RR=5.27). For officers, six Ranch Hands (2.2%) and two Comparisons (0.5%) had the MSK anti-smooth muscle antibody present. All other adjusted Model 1 contrasts were nonsignificant (Table 19-16(a,b): p>0.19). Both adjusted and unadjusted analyses of Model 2 were nonsignificant (Table 19-16(c,d): p>0.15 for both analyses).

The unadjusted analysis of Model 3 uncovered a significant difference in the presence of the MSK anti-smooth muscle antibody between Ranch Hands in the background dioxin category (1.9%) and Comparisons (0.7%) (Table 19-16(e): p=0.035, Unadjusted RR=3.22). After adjustment for covariates, the association remained significant (Table 19-16(f): p=0.021, Adjusted RR=3.91). All other Model 3 contrasts were nonsignificant in both the unadjusted and adjusted analyses (Table 19-16(e,f): p>0.30 for all other contrasts).

The Model 4 unadjusted analysis revealed a significant association between 1987 dioxin levels and the presence of the MSK anti-smooth muscle antibody (Table 19-16(g): p=0.029, Unadjusted RR=0.62). After adjustment for covariates, the association remained significant (Table 19-16(h): p=0.013, Adjusted RR=0.47). The percentages of Ranch Hands with the MSK anti-smooth muscle antibody were 2.5%, 0.4%, and 0.9% for the low, medium, and high 1987 dioxin categories, respectively.

Table 19-16. Analysis of Lupus Panel: MSK Anti-smooth Muscle Antibody

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*695*	*9 (1.3)*	*1.74 (0.67,4.53)*	*0.258*
	Comparison	*1,068*	*8 (0.7)*		
Officer	Ranch Hand	276	6 (2.2)	4.61 (0.92,23.01)	0.062
	Comparison	417	2 (0.5)		
Enlisted Flyer	Ranch Hand	116	1 (0.9)	0.48 (0.05,4.63)	0.522
	Comparison	167	3 (1.8)		
Enlisted Groundcrew	Ranch Hand	303	2 (0.7)	1.07 (0.18,6.41)	0.945
	Comparison	484	3 (0.6)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,756*	*1.90 (0.71,5.02)*	*0.199*
Officer	692	5.27 (1.04,26.82)	0.045*
Enlisted Flyer	282	0.46 (0.05,4.69)	0.516
Enlisted Groundcrew	782	1.20 (0.19,7.42)	0.845

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	123	1 (0.8)	0.46 (0.14,1.56)	0.158
Medium	128	2 (1.6)		
High	126	0 (0.0)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

n	Analysis Results for Log_2 (Initial Dioxin) Adjusted Relative Risk (95% C.I.)[a]	p-Value
376	0.56 (0.17,1.89)	0.277

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, current cigarette smoking, and the physical activity index because of the sparse number of Ranch Hands with the MSK anti-smooth muscle antibody present.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,068	8 (0.7)		
Background RH	317	6 (1.9)	3.22 (1.08,9.55)	0.035*
Low RH	187	3 (1.6)	2.04 (0.53,7.88)	0.300
High RH	190	0 (0.0)	--	0.483[c]
Low plus High RH	377	3 (0.8)	--	0.999[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with the MSK anti-smooth muscle antibody present.

*: Statistically significant (0.010<p-value≤0.050).

--: Results were not presented because of the sparse number of Ranch Hands with the MSK anti-smooth muscle antibody present.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 19-16. Analysis of Lupus Panel: MSK Anti-smooth Muscle Antibody (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,064		
Background RH	315	3.91 (1.23,12.42)	0.021*
Low RH	187	1.86 (0.47,7.39)	0.376
High RH	189	--	--
Low plus High RH	376	--	--

[a]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

--: Results were not presented because of the sparse number of Ranch Hands with the MSK anti-smooth muscle antibody present.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	242	6 (2.5)	0.62 (0.40,0.95)	0.029*
Medium	224	1 (0.4)		
High	228	2 (0.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
691	0.47 (0.26,0.85)	0.013*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Results were not adjusted for the physical activity index because of the sparse number of Ranch Hands with the MSK anti-smooth muscle antibody present.

19.2.2.1.14   Lupus Panel: MSK Anti-mitochondrial Antibody

Because of the sparse number of participants with the MSK anti-mitochondrial antibody present (2 Ranch Hands and 2 Comparisons), analysis was limited. All unadjusted and adjusted analyses performed for Models 1 through 4 were nonsignificant (Table 19-17(a-h): p>0.08 for all analyses).

Table 19-17. Analysis of Lupus Panel: MSK Anti-mitochondrial Antibody

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*695*	*2 (0.3)*	*1.54 (0.22,10.95)*	*0.668*
	Comparison	*1,068*	*2 (0.2)*		
Officer	Ranch Hand	276	2 (0.7)	3.04 (0.27,33.65)	0.365
	Comparison	417	1 (0.2)		
Enlisted Flyer	Ranch Hand	116	0 (0.0)	--	0.999[a]
	Comparison	167	1 (0.6)		
Enlisted Groundcrew	Ranch Hand	303	0 (0.0)	--	--
	Comparison	484	0 (0.0)		

[a]P-value was determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with the MSK anti-mitochondrial antibody present.

--:   Results were not presented because of the sparse number of participants with the MSK anti-mitochondrial antibody present.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,756*	*1.48 (0.20,10.71)*	*0.699*
Officer	692	3.02 (0.27,33.73)	0.369
Enlisted Flyer	282	--	--
Enlisted Groundcrew	782	--	--

--:   Results were not presented because of the sparse number of participants with the MSK anti-mitochondrial antibody present.

Note: Results were not adjusted for race, current alcohol use, and the physical activity index because of the sparse number of participants with the MSK anti-mitochondrial antibody present.

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin Category Summary Statistics				
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
Low	123	1 (0.8)	--	--
Medium	128	0 (0.0)		
High	126	0 (0.0)		

--: Results were not presented because of the sparse number of Ranch Hands with the MSK anti-mitochondrial antibody present.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)	p-Value
376	--	--

--: Results were not presented because of the sparse number of Ranch Hands with the MSK anti-mitochondrial antibody present.

Note: Adjusted analysis was not performed because of the sparse number of Ranch Hands with the MSK anti-mitochondrial antibody present.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,068	2 (0.2)		
Background RH	317	1 (0.3)	1.67 (0.15,18.95)	0.679
Low RH	187	1 (0.5)	2.87 (0.26,31.81)	0.391
High RH	190	0 (0.0)	--	0.999[c]
Low plus High RH	377	1 (0.3)	--	0.999[c]

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value was determined using a chi-square test with continuity correction because of the sparse number of Ranch Hands with the MSK anti-mitochondrial antibody present.

--: Results were not presented because of the sparse number of Ranch Hands with the MSK anti-mitochondrial antibody present.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,064		
Background RH	315	1.49 (0.13,17.51)	0.750
Low RH	187	2.48 (0.22,28.05)	0.463
High RH	189	--	--
Low plus High RH	376	--	--

[a]Relative risk and confidence interval relative to Comparisons.

--:   Results were not presented because of the sparse number of Ranch Hands with the MSK anti-mitochondrial antibody present.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

   Results were not adjusted for race, occupation, current alcohol use, and the physical activity index because of the sparse number of participants with the MSK anti-mitochondrial antibody present.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	242	1 (0.4)	0.51 (0.22,1.22)	0.141
Medium	224	1 (0.4)		
High	228	0 (0.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
691	0.45 (0.19,1.05)	0.084

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were only adjusted for age, body mass index, and lifetime alcohol history because of the sparse number of Ranch Hands with the MSK anti-mitochondrial antibody present.

19.2.2.1.15   Lupus Panel: MSK Anti-parietal Cell Antibody

Some of the analyses could not be adjusted for all covariates in Models 2 and 4 because of the sparse number of participants with the MSK anti-parietal cell antibody present. All unadjusted and adjusted analyses results for Models 1 through 4 of the MSK anti-parietal cell antibody were nonsignificant (Table 19-18(a-h): p≥0.09 for all analyses).

Table 19-18. Analysis of Lupus Panel: MSK Anti-parietal Cell Antibody

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*695*	*16 (2.3)*	*0.74 (0.40,1.35)*	*0.320*
	Comparison	*1,068*	*33 (3.1)*		
Officer	Ranch Hand	276	8 (2.9)	1.75 (0.63,4.88)	0.286
	Comparison	417	7 (1.7)		
Enlisted Flyer	Ranch Hand	116	1 (0.9)	0.28 (0.03,2.44)	0.250
	Comparison	167	5 (3.0)		
Enlisted Groundcrew	Ranch Hand	303	7 (2.3)	0.52 (0.22,1.24)	0.141
	Comparison	484	21 (4.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,756*	*0.73 (0.40,1.35)*	*0.310*
Officer	692	1.72 (0.62,4.84)	0.300
Enlisted Flyer	282	0.25 (0.03,2.18)	0.209
Enlisted Groundcrew	782	0.52 (0.22,1.25)	0.142

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	123	3 (2.4)	1.18 (0.70,1.98)	0.536
Medium	128	1 (0.8)		
High	126	3 (2.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
376	1.16 (0.66,2.05)	0.608

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race, military occupation, and the physical activity index because of the sparse number of Ranch Hands with the MSK anti-parietal cell antibody present.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,068	33 (3.1)		
Background RH	317	9 (2.8)	1.07 (0.50,2.28)	0.867
Low RH	187	4 (2.1)	0.66 (0.23,1.91)	0.446
High RH	190	3 (1.6)	0.44 (0.13,1.48)	0.186
Low plus High RH	377	7 (1.9)	0.54 (0.23,1.25)	0.152

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,064		
Background RH	315	1.26 (0.57,2.77)	0.568
Low RH	187	0.62 (0.21,1.81)	0.384
High RH	189	0.37 (0.11,1.26)	0.112
Low plus High RH	376	0.48 (0.21,1.12)	0.090

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	**n**	**Number (%) Present**	**Unadjusted Relative Risk (95% C.I.)[a]**	**p-Value**
Low	242	5 (2.1)	0.95 (0.70,1.30)	0.750
Medium	224	7 (3.1)		
High	228	4 (1.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
691	0.80 (0.54,1.19)	0.280

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Ranch Hands with the MSK anti-parietal cell antibody present.

19.2.2.1.16   Lupus Panel: Rheumatoid Factor

The analyses of Model 1 revealed a significant difference in the percentage of participants with a positive rheumatoid factor between Ranch Hands (22.5%) and Comparisons (16.1%) in the officer stratum. The analyses were significant both unadjusted and adjusted for covariates (Table 19-19(a,b): p=0.035, Unadjusted RR=1.51; p=0.028, Adjusted RR=1.55, respectively).

A significant inverse association was found between initial dioxin and the presence of a positive rheumatoid factor in both the unadjusted and adjusted Model 2 analyses (Table 19-19(c,d): p<0.001, Unadjusted RR=0.68; p<0.001, Adjusted RR=0.61, respectively). The percentage of Ranch Hands with the rheumatoid factor present were 30.9, 28.1, and 15.1 percent in the low, medium, and high initial dioxin categories, respectively.

The Model 3 unadjusted analysis revealed a significant difference in the percentage of participants with a positive rheumatoid factor between Ranch Hands in the low dioxin category (32.1%) and Comparisons (20.2%) (Table 19-19(e): p<0.001, Unadjusted RR=1.86). After adjustment for covariates, the difference remained significant (Table 19-19(f): p=0.001, Adjusted RR=1.81).

The Model 4 unadjusted analysis of the rheumatoid factor was not significant (Table 19-19(g): p=0.118, Unadjusted RR=0.92). After adjustment for covariates, however, the association became significant (Table 19-19(h): p=0.042, Adjusted RR=0.87). The percentages of Ranch Hands with the rheumatoid factor present were 21.9, 28.1, and 21.9 percent in the low, medium, and high 1987 dioxin categories, respectively.

Table 19-19. Analysis of Lupus Panel: Rheumatoid Factor

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*695*	*166 (23.9)*	*1.24 (0.98,1.56)*	*0.069*
	Comparison	*1,068*	*216 (20.2)*		
Officer	Ranch Hand	276	62 (22.5)	1.51 (1.03,2.22)	0.035*
	Comparison	417	67 (16.1)		
Enlisted Flyer	Ranch Hand	116	28 (24.1)	0.89 (0.51,1.54)	0.675
	Comparison	167	44 (26.3)		
Enlisted Groundcrew	Ranch Hand	303	76 (25.1)	1.21 (0.86,1.69)	0.272
	Comparison	484	105 (21.7)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,756*	*1.25 (0.99,1.58)*	*0.059*
Officer	692	1.55 (1.05,2.28)	0.028*
Enlisted Flyer	282	0.91 (0.52,1.59)	0.749
Enlisted Groundcrew	782	1.20 (0.85,1.69)	0.293

*: Statistically significant (0.010<p-value≤0.050).

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	123	38 (30.9)	0.68 (0.56,0.84)	<0.001**
Medium	128	36 (28.1)		
High	126	19 (15.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 19-19. Analysis of Lupus Panel: Rheumatoid Factor (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
376	0.61 (0.47,0.78)	<0.001**

[a]Relative risk for a twofold increase in initial dioxin.

**: Statistically significant (p-value≤0.010).

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,068	216 (20.2)		
Background RH	317	73 (23.0)	1.20 (0.89,1.63)	0.233
Low RH	187	60 (32.1)	1.86 (1.32,2.62)	<0.001**
High RH	190	33 (17.4)	0.82 (0.54,1.23)	0.328
Low plus High RH	377	93 (24.7)	1.23 (0.92,1.64)	0.158

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,064		
Background RH	315	1.33 (0.97,1.82)	0.075
Low RH	187	1.81 (1.28,2.57)	0.001**
High RH	189	0.74 (0.49,1.12)	0.156
Low plus High RH	376	1.15 (0.86,1.54)	0.336

[a]Relative risk and confidence interval relative to Comparisons.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
        Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 19-19. Analysis of Lupus Panel: Rheumatoid Factor (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Present	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	242	53 (21.9)	0.92 (0.82,1.02)	0.118
Medium	224	63 (28.1)		
High	228	50 (21.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
691	0.87 (0.77,1.00)	0.042*

[a]Relative risk for a twofold increase in 1987 dioxin.

*: Statistically significant (0.010<p-value≤0.050).

19.3   DISCUSSION

The human immune system comprises the immune-surveillance system, which fights invading organisms such as bacteria, viruses, and fungi. With the ability to distinguish foreign from self, the system detects and destroys aberrant cells, including cancer cells.

The two functions of the immune system are innate immunity and adaptive immunity. Innate immunity, similar in all humans, is the body's first response to an invading organism. When the body experiences a foreign organism, the immune system adapts and develops a specific response to that organism.

The adaptive immune system can be further broken down into cellular and humoral immunity. The cellular immune system comprises granulocytes and lymphocytes, whereas the humoral immune system comprises immunoglobulins and complement proteins. Granulocyte abnormalities are discussed in the assessment of the hematologic system (Chapter 16). The two major classes of lymphocytes, a type of WBC, are T cells and B cells. These cells and the interactions that take place between them are an integral part of the body's ability to recognize and destroy invading organisms or tumor cells. B cells eventually mature into plasma cells, which produce the immunoglobulins in the humoral immune system. The T cells, which comprise both helper and suppressor cell subtypes, help maintain a balance in the immune response. Another type of lymphocyte—the natural killer cell—is responsible for the surveillance and destruction of tumors. Natural killer cells have the ability to target foreign cells without assistance from other parts of the immune system (thus a "natural killer" cell).

When the body's immune response is altered, it is because of an immune deficiency or an exaggerated response to the system. Immune deficiencies can be inherited or acquired. Acquired deficiencies in the

immune system are most commonly associated with a decrease in immunoglobulins and, therefore, the humoral immune system. Increased activity in the humoral immune system is manifested by autoantibodies directed against various normal human cells, which can result in disorders such as rheumatoid arthritis and systemic lupus erythematosus. Deficiencies in the T-cell function in the cellular immune system, often seen in HIV patients or in patients undergoing chemotherapy, result in opportunistic organisms such as *Pneumocystis carinii* or fungal infections.

During the 2002 AFHS follow-up examination, numerous immunologic parameters were assessed. The dependent variables included the absolute lymphocyte count, cell surface marker studies for CD3+ cells (total T cells), CD4+ cells (helper T cells), CD8+ cells (suppressor T cells), CD20+ cells (B-cells), CD3+CD4+ helper T cells, and CD16+56+ natural killer cells. The humoral immune system was measured by examining the immunoglobulin levels for IgG, IgA, and IgM; increased activity in the immune system was measured by investigating a lupus panel, which included rheumatoid factor, the ANA test, the thyroid microsomal antibody test, the MSK anti-smooth muscle antibody, the MSK anti-mitochondrial antibodies, and the MSK anti-parietal cell antibodies.

A number of covariates were also examined, including age, race, military occupation, body mass index, current cigarette smoking, lifetime cigarette smoking, current alcohol use, lifetime alcohol use, and a physical activity index. Results of dependent variable and covariate associations were as expected and as found in other studies, such as CD3 cell counts increasing with age, cigarette smoking, and sedentary activity.

The immunologic evaluation performed on AFHS participants went far beyond the usual medical examinations used for routine general health assessments. As a test panel battery, this assessment provided an indepth and broad review of immunologic parameters designed to detect abnormalities or variances that may or may not be of clinical importance. Isolated significant differences were present, but none in a meaningful, clinically consistent manner that would indicate overt disease.

Analyses revealed a significant positive correlation between initial dioxin exposure and CD20+ cell counts. The adjusted means were similar for the medium and high initial dioxin categories, and both were greater than the low initial dioxin category.

Ranch Hands had a significantly decreased mean IgM level among enlisted flyers. While the difference was statistically significant, the clinical relevance is unknown.

In the lupus panel, a significant positive association was found between initial dioxin level and the presence of the ANA. The percentages of Ranch Hands with the ANA present, however, were 19.5, 11.7, and 27.8 percent in the low, medium, and high initial dioxin categories, respectively. There did not appear to be a dose-response effect.

Analyses of the rheumatoid factor and the anti-smooth muscle antibody revealed several significant differences, but the prevalence of abnormalities decreased as dioxin increased and the results were not supportive of a positive dose-response relation.

In conclusion, while there were some isolated significant differences in some categories of immune system measurements, none appeared to be consistent or of clinical significance. There was an increasing prevalence of a positive ANA with increasing initial dioxin levels. When looking at the individual autoantibodies, however, there were no consistent findings to support the presence of the ANA.

19.4   SUMMARY

The immunology assessment was based only on laboratory data. Associations with herbicide exposure (i.e., group – Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable in the immunology assessment. The significant adjusted results are discussed in the sections below.

19.4.1   Model 1: Group Analysis

The Model 1 adjusted analysis revealed significant findings for the analysis of certain military occupations for IgM, the MSK anti-smooth muscle antibody, and the rheumatoid factor. The mean IgM level was greater for Comparisons enlisted flyers than for Ranch Hand enlisted flyers. The significant results in the MSK anti-smooth muscle antibody test and in the rheumatoid factor test both occurred for officers. The MSK anti-smooth muscle analysis indicated that a greater percentage of Ranch Hand officers had the anti-smooth muscle antibody present than Comparison officers. Likewise, a greater percentage of Ranch Hand officers exhibited presence of a positive rheumatoid factor than Comparison officers. The results of the group analysis are provided in Table 19-20.

Table 19-20. Summary of Group Analysis (Model 1) for Immunology Variables (Ranch Hands vs. Comparisons)

| | UNADJUSTED | | | |
Variable	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Laboratory				
CD3+ Cells (T Cells) (C)	NS	NS	ns	NS
CD4+ Cells (Helper T Cells) (C)	NS	NS	ns	NS
CD8+ Cells (Suppressor Cells) (C)	NS	NS	ns	NS
CD16+56+ Cells (Natural Killer Cells) (C)	ns	ns	ns	NS
CD20+ Cells (B Cells) (C)	ns	ns	ns	NS
CD3+CD4+ Cells (Helper T Cells) (C)	NS	NS	ns	NS
Absolute Lymphocytes (C)	NS	ns	ns	NS
IgA (C)	ns	ns	ns	ns
IgG (C)	ns	ns	ns	ns
IgM (C)	ns	ns	p=0.020 (-15.54)	NS
Lupus Panel: ANA Test (D)	NS	ns	NS	NS
Lupus Panel: Thyroid Microsomal Antibody (D)	NS	NS	ns	NS
Lupus Panel: MSK Anti-smooth Muscle Antibody (D)	NS	NS	ns	NS
Lupus Panel: MSK Anti-mitochondrial Antibody (D)	NS	NS	ns	--
Lupus Panel: MSK Anti-parietal Cell Antibody (D)	ns	NS	ns	ns
Lupus Panel: Rheumatoid Factor (D)	NS	p=0.035 (1.51)	ns	NS

--: Analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
       C: Continuous dependent variable.
       D: Discrete dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

		ADJUSTED		
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Laboratory				
CD3+ Cells (T Cells) (C)	NS	NS	ns	NS
CD4+ Cells (Helper T Cells) (C)	NS	NS	ns	NS
CD8+ Cells (Suppressor Cells) (C)	NS	NS	ns	NS
CD16+56+ Cells (Natural Killer Cells) (C)	NS	ns	ns	NS
CD20+ Cells (B Cells) (C)	ns	ns	ns	ns
CD3+CD4+ Cells (Helper T Cells) (C)	NS	NS	ns	NS
Absolute Lymphocytes (C)	NS	ns	ns	NS
IgA (C)	ns	ns	ns	ns
IgG (C)	ns	ns	ns	NS
IgM (C)	ns	ns	p=0.031 (-13.82)	NS
Lupus Panel: ANA Test (D)	ns	ns	NS	NS
Lupus Panel: Thyroid Microsomal Antibody (D)	NS	NS	ns	NS
Lupus Panel: MSK Anti-smooth Muscle Antibody (D)	NS	p=0.045 (5.27)	ns	NS
Lupus Panel: MSK Anti-mitochondrial Antibody (D)	NS	NS	--	--
Lupus Panel: MSK Anti-parietal Cell Antibody (D)	ns	NS	ns	ns
Lupus Panel: Rheumatoid Factor (D)	NS	p=0.028 (1.55)	ns	NS

--: Analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
       C: Continuous dependent variable.
       D: Discrete dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

19.4.2 Model 2: Initial Dioxin Analysis

The Model 2 adjusted analysis revealed a significant association between CD20+ cell (B cell) counts and initial dioxin. The CD20+ cell count increased as initial dioxin increased. The associations between initial dioxin and both the overall ANA test and the rheumatoid factor were significant. For the ANA test, the percentage of Ranch Hands with the ANA present increased as initial dioxin increased. As initial dioxin increased, however, the percentage of Ranch Hands with a positive rheumatoid factor decreased. The results of the initial dioxin analysis are shown in Table 19-21.

Table 19-21. Summary of Initial Dioxin Analysis (Model 2) for Immunology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Laboratory		
CD3+ Cells (T Cells) (C)	NS	NS
CD4+ Cells (Helper T Cells) (C)	NS	NS
CD8+ Cells (Suppressor Cells) (C)	NS	NS
CD16+56+ Cells (Natural Killer Cells) (C)	ns	ns
CD20+ Cells (B Cells) (C)	p=0.001 (0.119)	p=0.016 (0.102)
CD3+CD4+ Cells (Helper T Cells) (C)	NS	NS
Absolute Lymphocytes (C)	p=0.029 (0.031)	NS
IgA (C)	NS	NS
IgG (C)	NS	ns
IgM (C)	NS	ns
Lupus Panel: ANA Test (D)	p=0.037 (1.22)	p=0.035 (1.28)
Lupus Panel: Thyroid Microsomal Antibody (D)	ns	ns
Lupus Panel: MSK Anti-smooth Muscle Antibody (D)	ns	ns
Lupus Panel: MSK Anti-mitochondrial Antibody (D)	--	--
Lupus Panel: MSK Anti-parietal Cell Antibody (D)	NS	NS
Lupus Panel: Rheumatoid Factor (D)	p<0.001 (0.68)	p<0.001 (0.61)

--: Analysis was not performed because of the sparse number of Ranch Hands with an abnormality.

Note: NS or ns: Not significant (p>0.05).
     C: Continuous dependent variable.
     D: Discrete dependent variable.

     The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

     A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

19.4.3 Model 3: Categorized Dioxin Analysis

Results for the Model 3 adjusted analysis revealed the presence of the MSK anti-smooth muscle antibody in a significantly higher percentage of Ranch Hands in the background dioxin category than Comparisons. In addition, the adjusted analysis indicated presence of a positive rheumatoid factor in a significantly higher percentage of Ranch Hands in the low dioxin category than Comparisons. The results of the categorized dioxin analysis are presented in Table 19-22.

Table 19-22. Summary of Categorized Dioxin Analysis (Model 3) for Immunology Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	Low Ranch Hands vs. Comparisons	High Ranch Hands vs. Comparisons	Low plus High Ranch Hands vs. Comparisons
Laboratory				
CD3+ Cells (T Cells) (C)	ns	NS	p=0.036 (130.6)	NS
CD4+ Cells (Helper T Cells) (C)	ns	NS	p=0.036 (90.4)	NS
CD8+ Cells (Suppressor Cells) (C)	ns	NS	NS	NS
CD16+56+ Cells (Natural Killer Cells) (C)	ns	NS	ns	NS
CD20+ Cells (B Cells) (C)	ns	p=0.016 (-34.1)	p=0.047 (32.7)	ns
CD3+CD4+ Cells (Helper T Cells) (C)	ns	NS	p=0.026 (92.5)	NS
Absolute Lymphocytes (C)	ns	ns	p=0.017 (129.6)	NS
IgA (C)	ns	NS	ns	NS
IgG (C)	p=0.045 (-34.6)	NS	ns	ns
IgM (C)	ns	ns	ns	ns
Lupus Panel: ANA Test (D)	ns	ns	NS	NS
Lupus Panel: Thyroid Microsomal Antibody (D)	NS	NS	NS	NS
Lupus Panel: MSK Anti-smooth Muscle Antibody (D)	p=0.035 (3.22)	NS	ns	NS
Lupus Panel: MSK Anti-mitochondrial Antibody (D)	NS	NS	ns	NS
Lupus Panel: MSK Anti-parietal Cell Antibody (D)	NS	ns	ns	ns
Lupus Panel: Rheumatoid Factor (D)	NS	p<0.001 (1.86)	ns	NS

Note: NS or ns: Not significant (p>0.05).
　　　　C: Continuous dependent variable.
　　　　D: Discrete dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

Table 19-22. Summary of Categorized Dioxin Analysis (Model 3) for Immunology Variables (Ranch Hands vs. Comparisons) (Continued)

	ADJUSTED			
Variable	**Background Ranch Hands vs. Comparisons**	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Laboratory				
CD3+ Cells (T Cells) (C)	NS	NS	NS	NS
CD4+ Cells (Helper T Cells) (C)	ns	NS	NS	NS
CD8+ Cells (Suppressor Cells) (C)	NS	NS	NS	NS
CD16+56+ Cells (Natural Killer Cells) (C)	ns	NS	ns	NS
CD20+ Cells (B Cells) (C)	ns	ns	NS	ns
CD3+CD4+ Cells (Helper T Cells) (C)	ns	NS	NS	NS
Absolute Lymphocytes (C)	ns	ns	NS	NS
IgA (C)	ns	NS	ns	NS
IgG (C)	ns	ns	ns	ns
IgM (C)	ns	ns	ns	ns
Lupus Panel: ANA Test (D)	ns	ns	NS	NS
Lupus Panel: Thyroid Microsomal Antibody (D)	NS	NS	NS	NS
Lupus Panel: MSK Anti-smooth Muscle Antibody (D)	p=0.021 (3.91)	NS	--	--
Lupus Panel: MSK Anti-mitochondrial Antibody (D)	NS	NS	--	--
Lupus Panel: MSK Anti-parietal Cell Antibody (D)	NS	ns	ns	ns
Lupus Panel: Rheumatoid Factor (D)	NS	p=0.001 (1.81)	ns	NS

--: Analysis was not performed because of the sparse number of participants with an abnormality.

Note: NS or ns: Not significant (p>0.05).
　　　　C: Continuous dependent variable.
　　　　D: Discrete dependent variable.

　　　　The p-value was given if $p \leq 0.05$. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

　　　　A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

19.4.4   Model 4: 1987 Dioxin Level Analysis

The Model 4 adjusted analysis uncovered significant associations between 1987 dioxin levels and the MSK anti-smooth muscle antibody and the rheumatoid factor. Both the percentage of Ranch Hands with presence of the MSK anti-smooth muscle antibody and the percentage of Ranch Hands with presence of a positive rheumatoid factor decreased as the 1987 dioxin levels increased. The results of the 1987 dioxin analysis are displayed in Table 19-23.

Table 19-23. Summary of 1987 Dioxin Analysis (Model 4) for Immunology Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Laboratory		
CD3+ Cells (T Cells) (C)	NS	NS
CD4+ Cells (Helper T Cells) (C)	NS	NS
CD8+ Cells (Suppressor Cells) (C)	NS	NS
CD16+56+ Cells (Natural Killer Cells) (C)	NS	ns
CD20+ Cells (B Cells) (C)	p=0.042 (0.046)	NS
CD3+CD4+ Cells (Helper T Cells) (C)	NS	NS
Absolute Lymphocytes (C)	p=0.029 (0.021)	ns
IgA (C)	NS	NS
IgG (C)	NS	ns
IgM (C)	ns	ns
Lupus Panel: ANA Test (D)	NS	NS
Lupus Panel: Thyroid Microsomal Antibody (D)	NS	NS
Lupus Panel: MSK Anti-smooth Muscle Antibody (D)	p=0.029 (0.62)	p=0.013 (0.47)
Lupus Panel: MSK Anti-mitochondrial Antibody (D)	ns	ns
Lupus Panel: MSK Anti-parietal Cell Antibody (D)	ns	ns
Lupus Panel: Rheumatoid Factor (D)	ns	p=0.042 (0.87)

Note: NS or ns: Not significant (p>0.05).
　　　　C: Continuous dependent variable.
　　　　D: Discrete dependent variable.

　　　　The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

　　　　A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

19.4.5 Summary of Significant Results

Table 19-24 summarizes the significant results (p≤0.05) for the adjusted analyses that were performed for the immunology assessment. The dependent variable and its table reference are listed along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and is explained in footnotes.

Table 19-24. Summary of Results from Significant Adjusted Analyses in the Immunology Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
CD20+ Cells (B Cells) (19-8)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.016	0.102 (0.042)	Low: 187.2 cells/mm^3 Medium: 263.8 cells/mm^3 High: 257.7 cells/mm^3	(a)
IgM (19-13)	1	RH vs. C: Enlisted Flyer	0.031	-13.82	RH: 80.01 mg/dL C: 93.83 mg/dL	(b)
Lupus Panel: ANA Test (19-14)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.035	1.28 (1.02,1.61)	Low: 19.5% Medium: 11.7% High: 27.8%	(c)
Lupus Panel: MSK Smooth Muscle Antibody (19-16)	1	RH vs. C, Officer	0.045	5.27 (1.04,26.8)	RH: 2.2% C: 0.5%	(d)
	3	Background RH vs. C	0.021	3.91 (1.23,12.4)	RH: 1.9% C: 0.7%	(e)
	4	All RH: 1987 Dioxin	0.013	0.47 (0.26,0.85)	Low: 2.5% Medium: 0.4% High: 0.9%	(f)
Lupus Panel: Rheumatoid Factor (19-19)	1	RH vs. C, Officer	0.028	1.55 (1.05,2.28)	RH: 22.5% C: 16.1%	(d)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin	<0.001	0.61 (0.47,0.78)	Low: 30.9% Medium: 28.1% High: 15.1%	(c)
	3	Low RH vs. C	0.001	1.81 (1.28,2.57)	RH: 32.1% C: 20.2%	(e)
	4	All RH: 1987 Dioxin	0.042	0.87 (0.77,1.00)	Low: 21.9% Medium: 28.1% High: 21.9%	(f)

(a): Continuous variable: slope and standard error were presented and were based on natural logarithm of dependent variable versus $\log_2$ (initial dioxin); adjusted means were presented for each of three initial dioxin categories.

(b): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each exposure group in contrast.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal was presented for each of three initial dioxin categories.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(e): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(f): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

Note: RH = Ranch Hand.
         C = Comparison.

      Model 2:   Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt. (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt)

      Model 3:   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
                      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
                      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

      Model 4:   Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt. (Ranch Hands only)

19.5 CONCLUSION

The immunologic evaluation performed on AFHS participants provided an indepth and broad review of immunologic parameters designed to detect abnormalities or variances that may or may not carry clinical importance. Analyses revealed a significant positive correlation between initial dioxin exposure and CD20+ cell counts and a significantly lower mean IgM level for Ranch Hand enlisted flyers.

In the lupus panel, a significant positive association was found between initial dioxin level and the presence of the ANA, but the association did not appear to support a dose-response relation. Analyses of the rheumatoid factor and the anti-smooth muscle antibody revealed several significant differences, but the prevalence of abnormalities decreased as dioxin increased.

There was an increasing prevalence of a positive ANA in Ranch Hands with increasing initial dioxin levels. When looking at the individual autoantibodies, however, there were no consistent findings to support the presence of the ANA. While there were some isolated significant differences in some categories of immune system measurements, there was nothing that appeared to be consistent or of clinical significance.

REFERENCES

1. Salvaggio, J.E., and K.A. Sullivan. 1998. The immune system and the environment. In: Environmental and Occupational Medicine. W.N. Rom, ed. 3rd ed. Lippincott-Raven: Philadelphia, PA.

2. Vos, J.G., J.A. Moore, and J.G. Zinkl. 1973. Effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin on the immune system of laboratory animals. *Environmental Health Perspectives* 5:149-62.

3. Harris, M.W., J.A. Moore, J.G. Vos, and B.N. Gupta. 1972. General biological effects of TCDD in laboratory animals. *Environmental Health Perspectives* 5:101-9.

4. Kociba, R.J., P.A. Keeler, C.N. Park, and P.J. Gehring. 1976. 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD): Results of a 13-week oral toxicity study in rats. *Toxicology and Applied Pharmacology* 35:553-74.

5. Gupta, B.N., J.G. Vos, J.A. Moore, J.G. Zinkl, and B.C. Bullock. 1973. Pathologic effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin in laboratory animals. *Environmental Health Perspectives* 5:125-40.

6. Thomas, P.T., and R.D. Hinsdill. 1979. The effect of perinatal exposure to tetrachlorodibenzo-p-dioxin on the immune response of young mice. *Drug and Chemical Toxicology* 2:77-98.

7. Luster, M.I., G.A. Boorman, J.H. Dean, M.W. Harris, R.W. Luebke, M.L. Padarathsingh, and J.A. Moore. 1980. Examination of bone marrow, immunologic parameters and host susceptibility following pre- and postnatal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *International Journal of Immunopharmacology* 2:301-10.

8. White, K.L., Jr., H.H. Lysy, J.A. McCay, and A.C. Anderson. 1986. Modulation of serum complement levels following exposure to polychlorinated dibenzo-p-dioxins. *Toxicology and Applied Pharmacology* 84:209-19.

9. Thigpen, J.E., R.E. Faith, E.E. McConnell, and J.A. Moore. 1975. Increased susceptibility to bacterial infection as a sequela of exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Infection and Immunity* 12:1319-24.

10. Hinsdill, R.D., D.L. Couch, and R.S. Speirs. 1980. Immunosuppression in mice induced by dioxin (TCDD) in feed. *Journal of Environmental Pathology and Toxicology* 4:401-25.

11. Sugita-Konishi, Y., K. Kobayashi, H. Naito, K. Miura, and Y. Suzuki. 2003. Effect of lactational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin on the susceptibility to Listeria infection. *Bioscience, Biotechnology and Biochemistry* 67:89-93.

12. Tucker, A.N., S.J. Vore, and M.I. Luster. 1986. Suppression of B-cell differentiation by 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Molecular Pharmacology* 29:372-7.

13. House, R.V., L.D. Lauer, M.J. Murray, P.T. Thomas, J.P. Ehrlich, G.R. Burleson, and J.H. Dean. 1990. Examination of immune parameters and host resistance mechanisms in B6C3F1 mice following adult exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 31:203-15.

14. Clark, D.A., G. Sweeney, S. Safe, E. Hancock, D.G. Kilburn, and J. Gauldie. 1983. Cellular and genetic basis for suppression of cytotoxic T-cell generation by haloaromatic hydrocarbons. *Immunopharmacology* 6:143-53.

15. Nohara, K., H. Izumi, S. Tamura, R. Nagata, and C. Tohyama. 2002. Effect of low-dose 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on influenza A virus-induced mortality in mice. *Toxicology* 170:131-8.

16. Vorderstrasse, B.A., A.A. Bohn, and B.P. Lawrence. 2003. Examining the relationship between impaired host resistance and altered immune function in mice treated with TCDD. *Toxicology* 188:15-28.

17. Holsapple, M.P., D.L. Morris, S.C. Wood, and N.K. Snyder. 1991. 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced changes in immunocompetence: Possible mechanisms. *Annual Review of Pharmacology and Toxicology* 31:73-100.

18. Vos, J.G., H. Van Loveren, and H.J. Schuurman. 1991. Immunotoxicity of dioxin: Immune function and host resistance in laboratory animals and humans. In: Biological Basis for Risk Assessment of Dioxins and Related Compounds. M.A. Gallo, R.J. Scheuplein, and K.A. van der Heijden, eds. Cold Spring Harbor Laboratory Press: Plainview, NY.

19. Schuurman, H.J., H. Van Loveren, J. Rozing, and J.G. Vos. 1992. Chemicals trophic for the thymus: Risk for immunodeficiency and autoimmunity. *International Journal of Immunopharmacology* 14:369-75.

20. Iverson F., and D.L. Grant. 1991. Toxicology of the polychlorinated biphenyls, dibenzofurans, and dibenzodioxins. In: Environmental Carcinogens: Methods of Analysis and Exposure Measurement: Polychlorinated Dioxins and Dibenzofurans. C. Rappe, H.R. Buser, B. Dodet, and I. K. O'Neill, eds. International Agency for Research on Cancer: Lyon, France.

21. Kerkvliet, N., and G.R. Burleson. 1994. Immunotoxicity of TCDD and related halogenated aromatic hydrocarbons. In: Immunotoxicology and Immunopharmacology. J.H. Dean, M.I. Luster, and A.E. Munson, eds. 2nd ed. Raven Press: New York, NY.

22. Birnbaum, L.S., and J. Tuomisto. 2000. Non-carcinogenic effects of TCDD in animals. *Food Additives and Contaminants* 17:275-88.

23. Holsapple, M.P., N.K. Snyder, S.C. Wood, and D.L. Morris. 1991. A review of 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced changes in immunocompetence: 1991 update. *Toxicology* 69:219-55.

24. Blaylock, B.L., S.D. Holladay, C.E. Comment, J.J. Heindel,, and M.I. Luster. 1992. Exposure to tetrachlorodibenzo-p-dioxin (TCDD) alters fetal thymocyte maturation. *Toxicology and Applied Pharmacology* 112:207-13.

25. Holladay, S.D., P. Lindstrom, B.L. Blaylock, C.E. Comment, D.R. Germolec, J.J. Heindell, and M.I. Luster. 1991. Perinatal thymocyte antigen expression and postnatal immune development altered by gestational exposure to tetrachlorodibenzo-p-dioxin (TCDD). *Teratology* 44:385-93.

26. Luster, M.I., S.D. Holladay, B.L. Blaylock, D. Germolec, G. Clark, C.E. Comment, J. Heindel, and G.J. Rosenthal. 1992. TCDD inhibits murine thymocyte and B lymphocyte maturation. *Chemosphere* 25:115-8.

27. de Waal, E.J., L.H. Rademakers, H.J. Schuurman, and H. van Loveren. 1993. Ultrastructure of interdigitating cells in the rat thymus during cyclosporin A treatment. *Advances in Experimental Medicine and Biology* 329:153-7.

28. Vos, J.G., and J.A. Moore. 1974. Suppression of cellular immunity in rats and mice by maternal treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *International Archives of Allergy and Applied Immunology* 47:777-94.

29. Faith, R.E., and J.A. Moore. 1977. Impairment of thymus-dependent immune functions by exposure of the developing immune system to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Journal of Toxicology and Environmental Health* 3:451-64.

30. Vecchi, A., A. Mantovani, M. Sironi, W. Luini, F. Spreafico, and S. Garattini. 1980. The effect of acute administration of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on humoral antibody production and cell-mediated activities in mice. *Archives of Toxicology Supplement* 4:163-5.

31. Clark, D.A., J. Gauldie, M.R. Szewczuk, and G. Sweeney. 1981. Enhanced suppressor cell activity as a mechanism of immunosuppression by 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Proceedings of the Society for Experimental Biology and Medicine* 168:290-9.

32. Holsapple, M.P., P.J. McNerney, D.W. Barnes, and K.L. White, Jr. 1984. Suppression of humoral antibody production by exposure to 1,2,3,6,7,8-hexachlorodibenzo-p-dioxin. *Journal of Pharmacology and Experimental Therapeutics* 231:518-26.

33. Kerkvliet, N.I., J.A. Brauner, and J.P. Matlock. 1985. Humoral immunotoxicity of polychlorinated diphenyl ethers, phenoxyphenols, dioxins and furans present as contaminants of technical grade pentachlorophenol. *Toxicology* 36:307-24.

34. Morris, D.L., N.K. Snyder, V. Gokani, R.E. Blair, and M.P. Holsapple. 1992. Enhanced suppression of humoral immunity in DBA/2 mice following subchronic exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicology and Applied Pharmacology* 112:128-32.

35. Nohara, K., H. Fujimaki, S. Tsukumo, K. Inouye, H. Sone, and C. Tohyama. 2002. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on T-cell-derived cytokine production in ovalbumin (OVA)-immunized C57Bl/6 mice. *Toxicology* 172:49-58.

36. Ito, T., K. Inouye, H. Fujimaki, C. Tohyama, and K. Nohara. 2002. Mechanism of TCDD-induced suppression of antibody production: Effect on T-cell-derived cytokine production in the primary immune reaction of mice. *Toxicological Sciences* 70:46-54.

37. Luster, M.I., L.H. Hong, G.A. Boorman, G. Clark, H.T. Hayes, W.F. Greenlee, K. Dold, and A.N. Tucker. 1985. Acute myelotoxic responses in mice exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Toxicology and Applied Pharmacology* 81:156-65.

38. Chastain, J.E., Jr., and T.L. Pazdernik. 1985. 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)-induced immunotoxicity. *International Journal of Immunopharmacology* 7:849-56.

39. Fine, J.S., T.A. Gasiewicz, and A.E. Silverstone. 1989. Lymphocyte stem cell alterations following perinatal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Molecular Pharmacology* 35:18-25.

40. Luster, M.I., D.R. Germolec, G. Clark, G. Wiegand, and G.J. Rosenthal. 1988. Selective effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin and corticosteroid on in vitro lymphocyte maturation. *Journal of Immunology* 140:928-35.

41. White, K.L., Jr., and A.C. Anderson. 1985. Suppression of mouse complement activity by contaminants of technical grade pentachlorophenol. *Agents and Actions* 16:385-92.

42. Lin, W.Q., and K.L. White, Jr. 1993. Production of complement component C3 in vivo following 2,3,7,8-tetrachlorodibenzo-p-dioxin exposure. *Journal of Toxicology and Environmental Health* 39:273-85.

43. Lin, W.Q., and K.L. White, Jr. 1993. Mouse Hepa 1c1c7 hepatoma cells produce complement component C3; 2,3,7,8-tetrachlorodibenzo-p-dioxin fails to modulate this capacity. *Journal of Toxicology and Environmental Health* 39:27-41.

44.   Poland, A., E. Glover, and A.S. Kende. 1976. Stereospecific, high affinity binding of 2,3,7,8-tetrachlorodibenzo-p-dioxin by hepatic cytosol. Evidence that the binding species is receptor for induction of aryl hydrocarbon hydroxylase. *Journal of Biological Chemistry* 251:4936-46.

45.   Poland, A., and J.C. Knutson. 1982. 2,3,7,8-tetrachlorodibenzo-p-dioxin and related halogenated aromatic hydrocarbons: Examination of the mechanism of toxicity. *Annual Review of Pharmacology and Toxicology* 22:517-54.

46.   Okey, A.B., D.S. Riddick, and P.A. Harper. 1994. The Ah-receptor: Mediator of the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. *Toxicology Letters* 70:1-22.

47.   Silbergeld, E.K., and T.A. Gasiewicz,. 1989. Dioxins and the Ah-receptor. *American Journal of Industrial Medicine* 16:455-74.

48.   Kerkvliet, N.I. 2002. Recent advances in understanding the mechanisms of TCDD immunotoxicity. *International Immunopharmacology* 2:277-91.

49.   Silkworth, J.B., L.A. Antrim, and G. Sack. 1986. Ah-receptor mediated suppression of the antibody response in mice is primarily dependent on the Ah phenotype of lymphoid tissue. *Toxicology and Applied Pharmacology* 86:380-90.

50.   Holsapple, M.P., N.K. Snyder, V. Gokani, R.E. Blair, and D.L. Morris. 1991. Role of Ah-receptor in suppression of in vivo antibody response by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is dependent on exposure conditions. *Federation of American Societies for Experimental Biology Journal* 5:A508.

51.   Davis, D., and S. Safe. 1991. Halogenated aryl hydrocarbon-induced suppression of the in vitro plaque-forming cell response to sheep red blood cells is not dependent on the Ah-receptor. *Immunopharmacology* 21:183-90.

52.   Davis, D., and S. Safe. 1990. Immunosuppressive activities of polychlorinated biphenyls in C57BL/6N mice: Structure-activity relationships as Ah-receptor agonists and partial antagonists. *Toxicology* 63:97-111.

53.   Vecchi, A., M. Sironi, M.A. Canegrati, M. Recchia, and S. Garattini. 1983. Immunosuppressive effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin in strains of mice with different susceptibility to induction of aryl hydrocarbon hydroxylase. *Toxicology and Applied Pharmacology* 68:434-41.

54.   Kerkvliet, N.I., L.B. Steppan, J.A. Brauner, J.A. Deyo,, M.C. Henderson, R.S. Tomar, and D.R. Buhler. 1990. Influence of the Ah locus on the humoral immunotoxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin: Evidence for Ah-receptor-dependent and Ah-receptor-independent mechanisms of immunosuppression. *Toxicology and Applied Pharmacology* 105:26-36.

55.   Vorderstrasse, B.A., L.B. Steppan, A.E. Silverstone, and N.I. Kerkvliet. 2001. Aryl hydrocarbon receptor-deficient mice generate normal immune responses to model antigens and are resistant to TCDD-induced immune suppression. *Toxicology and Applied Pharmacology* 171:157-64.

56.   Kerkvliet, N.I., L. Baecher-Steppan, B.B. Smith, J.A. Youngberg, M.C. Henderson, and D.R. Buhler. 1990. Role of the Ah locus in suppression of cytotoxic T lymphocyte activity by halogenated aromatic hydrocarbons (PCBs and TCDD): Structure-activity relationships and effects in C57Bl/6 mice congenic at the Ah locus. *Fundamental and Applied Toxicology* 14:532-41.

57.   Pavlyak, A.L., S.M. Wielgosz, and E. Huttner. 1989. Proliferation of splenic lymphocytes is inhibited more strongly by 2,3,7,8-tetrachlorodibenzo-p-dioxin in C57BL/10 (Ah+Ah+) mice than in DBA/2 (Ah-Ah-) mice. *Bulletin for Experimental Biology and Medicine* 107:365-6.

58. Doi, H., T. Baba, C. Tohyama, and K. Nohara. 2003. Functional activation of arylhydrocarbon receptor (AhR) in primary T cells by 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Chemosphere* 52:655-62.

59. Lysy, H.H., J.A. McCay, and K.L. White, Jr. 1986. A structure activity relationship of dioxin suppression of complement activity and segregation with the Ah locus. *Toxicologist* 6:171.

60. Wagner, E., M.M. Frank, and R.J. Smialowicz. 2001. 2,3,7,8-tetrachlorodibenzo-p-dioxin and natural immunity: Lack of an effect on the complement system in a guinea pig model. *Toxicology* 159:107-13.

61. Dooley, R.K., and M.P. Holsapple. 1987. The primary cellular target responsible for tetrachlorodibenzo-p-dioxin (TCDD) induced immunosuppression is the B-lymphocyte. *Federation Proceedings* 46:151.

62. Kramer, C.M., K.W. Johnson, R.K. Dooley, and M.P. Holsapple. 1987. 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) enhances antibody production and protein kinase activity in murine B-cells. *Biochemical and Biophysical Research Communications* 145:25-33.

63. Neubert, R., U. Jacob-Muller, R. Stahlmann, H. Helge, and D. Neubert. 1990. Polyhalogenated dibenzo-p-dioxins and dibenzofurans and the immune system. 1. Effects on peripheral lymphocyte subpopulations of a non-human primate (*Callithrix jacchus*) after treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Archives of Toxicology* 64:345-59.

64. Neubert, R., U. Jacob-Muller, H. Helge, R. Stahlmann, and D. Neubert. 1991. Polyhalogenated dibenzo-p-dioxins and dibenzofurans and the immune system. 2. In vitro effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on lymphocytes of venous blood from man and a non-human primate (*Callithrix jacchus*). *Archives of Toxicology* 65:213-9.

65. Neubert, R., G. Golor, R. Stahlmann, H. Helge, and D. Neubert. 1992. Polyhalogenated dibenzo-p-dioxins and dibenzofurans and the immune system. 4. Effects of multiple-dose treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on peripheral lymphocyte subpopulations of a non-human primate (*Callithrix jacchus*). *Archives of Toxicology* 66:250-9.

66. Neubert, R., G. Golor, R. Stahlmann, H. Helge, and D. Neubert. 1992. Dose-dependent TCDD-induced increase or decrease in T-lymphocyte subsets in the blood of new world monkeys (*Callithrix jacchus*). *Chemosphere* 25:1201-6.

67. Neubert, R., H. Helge, and D. Neubert. 1995. Proliferative capacity of marmoset lymphocytes after tetanus vaccination and lack of 2,3,7,8-tetrachlorodibenzo-p-dioxin to reduce a booster effect. *Life Sciences* 56:437-44.

68. Hong, R. 1991. Effects of environmental toxins on lymphocyte function: Studies in rhesus and man. *Annals of Allergy* 66:474-80.

69. Roberts, E.A., K.C. Johnson, P.A. Harper, and A.B. Okey. 1990. Characterization of the Ah-receptor mediating aryl hydrocarbon hydroxylase induction in the human liver cell line HEp G2. *Archives of Biochemistry and Biophysics* 276:442-50.

70. Lorenzen, A., and A.B. Okey. 1991. Detection and characterization of Ah-receptor in tissue and cells from human tonsils. *Toxicology and Applied Pharmacology* 107:203-14.

71. Wang, X., M. Santostefano, Y. Lu, and S. Safe. 1992. A comparison of the mouse versus human aryl hydrocarbon (Ah) receptor complex: Effects of proteolysis. *Chemico-Biological Interactions* 85:79-93.

72. Wood, S.C., H.G. Jeong, D.L. Morris, and M.P. Holsapple. 1993. Direct effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on human tonsillar lymphocytes. *Toxicology* 81:131-43.

73. Wood, S.C., and M.P. Holsapple. 1993. Direct suppression of superantigen-induced IgM secretion in human lymphocytes by 2,3,7,8-TCDD. *Toxicology and Applied Pharmacology* 122:308-13.

74. Mehta, S., A. Holm, T. Mezzanotti, and R.N. Kurl. 1992. Effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on human lymphocyte maturation. *Chemosphere* 25:1095-9.

75. Neubert, R., L. Maskow, J. Webb, U. Jacob-Muller, A.C. Nogueira, I. Delgado, H. Helge, and D. Neubert. 1993. Chlorinated dibenzo-p-dioxins and dibenzofurans and the human immune system. 1. Blood cell receptors in volunteers with moderately increased body burdens. *Life Sciences* 53:1995-2006.

76. Neubert, R., L. Maskow, I. Delgado, H. Helge, and D. Neubert. 1995. Chlorinated dibenzo-p-dioxins and dibenzofurans and the human immune system. 2. In vitro proliferation of lymphocytes from workers with quantified moderately increased body burdens. *Life Sciences* 56:421-36.

77. Knutsen, A.P. 1984. Immunologic effects of TCDD exposure in humans. *Bulletin of Environmental Contamination and Toxicology* 33:673-81.

78. Hoffman, R.E., P.A. Stehr-Gree, K.B. Webb, R.G. Evans, A.P. Knutsen, W.F. Schramm, J.L. Staake, B.B. Gibson, and K.K. Steinberg. 1986. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *The Journal of the American Medical Association* 255:2031-8.

79. Knutsen, A.P., S.T. Roodman, R.G. Evans, K.R. Mueller, K.B. Webb, P. Stehr-Green, R.E. Hoffman, and W.F. Schramm. 1987. Immune studies in dioxin-exposed Missouri residents: Quail Run. *Bulletin of Environmental Contamination and Toxicology* 39:481-9.

80. Evans, R.G., K.B. Webb, A.P. Knutsen, S.T. Roodman, D.W. Roberts, J.R. Bagby, W.A. Garrett, Jr., and J.S. Andrews, Jr. 1988. A medical follow-up of the health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Archives of Environmental Health* 43:273-8.

81. Stehr, P.A., G. Stein, K. Webb, W. Schramm, W.B. Gedney, H.D. Donnell, S. Ayres, H. Falk, E. Sampson, and S.J. Smith. 1986. A pilot epidemiologic study of possible health effects associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin contaminations in Missouri. *Archives of Environmental Health* 41:16-22.

82. Webb, K., R.G. Evans, P. Stehr, and S.M. Ayres. 1987. Pilot study on health effects of environmental 2,3,7,8-TCDD in Missouri. *American Journal of Industrial Medicine* 11:685-91.

83. Stehr-Green, P.A., R.E. Hoffman, K. Webb, R.G. Evans, A.P. Knutsen, W. Schramm, J.L. Staake, B.B. Gibson, and K.K. Steinberg. 1987. Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Chemosphere* 16:2089-94.

84. Webb, K.B., R.G. Evans, A.P. Knutsen, S.T. Roodman, D.W. Roberts, W.F. Schramm, B.B. Gibson, J.S. Andrews, Jr., L.L. Needham, and D.G. Patterson. 1989. Medical evaluation of subjects with known body levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 28:183-93.

85. Patterson D.G., R.E. Hoffman, L.L Needham, D.W. Roberts, J.R. Bagby, J.L. Pirkle, H. Falk, E.J. Sampson, and V.N. Houk. 1986. 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in adipose tissue of exposed and control persons in Missouri: An interim report. *The Journal of the American Medical Association* 256:2683-6.

86. Stehr-Green, P.A., P.H. Naylor, and R.E. Hoffman. 1989. Diminished thymosin alpha-1 levels in persons exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Journal of Toxicology and Environmental Health* 28:285-95.

87. Reggiani, G. 1978. Medical problems raised by the TCDD contamination in Seveso, Italy. *Archives of Toxicology* 40:161-88.

88. Pocchiari, F., V. Silano, and A. Zampieri. 1979. Human health effects from accidental release of tetrachlorodibenzo-p-dioxin (TCDD) at Seveso, Italy. *Annals of the New York Academy of Sciences* 320:311-20.

89. Sirchia, G.G. 1980. Exposure to TCDD: Immunologic effects. NRC Workshop: Plans for clinical and epidemiologic follow-up after area-wide chemical contamination. National Academy Press: Washington, DC.

90. Ghezzi, I., P. Cannatelli, G. Assennato, F. Merlo, P. Mocarelli, P. Brambilla, and F. Sicurello. 1982. Potential 2,3,7,8-tetrachlorodibenzo-p-dioxin exposure of Seveso decontamination workers: A controlled prospective study. *Scandinavian Journal of Work, Environment and Health* 8(Suppl 1):176-9.

91. Tognoni, G., and A. Bonaccorsi. 1982. Epidemiological problems with TCDD (a critical view). *Drug Metabolism Reviews* 13:447-69.

92. Mocarelli, P., A. Marocchi, P. Brambilla, P. Gerthoux, L. Colombo, A. Mondonico, and L. Meazza. 1991. Effects of dioxin exposure in humans at Seveso, Italy. In: Banbury Report 35: Biological basis for risk assessment of dioxins and related compounds. M.A. Gallo, R.J. Scheuplein, and K.A. van der Heijden, eds. Cold Spring Harbor Laboratory Press: Plainview, NY.

93. Mocarelli, P., A. Marocchi, P. Brambilla, P. Gerthoux, C. Beretta, L. Colombo, M. Bertona, C. Sarto, P. Tramacere, A. Mondonico, C. Crespi, S. Signorini, and R. Brivio. 1992. Human data derived from the Seveso accident -- relevance for human risk assessment. *Toxic Substances Journal* 12:151-73.

94. Baccarelli, A., P. Mocarelli, D.G. Patterson, Jr., M. Bonzini, A.C. Pesatori, N. Caporaso, and M.T. Landi. 2002. Immunologic effects of dioxin: New results from Seveso and comparison with other studies. *Environmental Health Perspectives* 110:1169-73.

95. May, G. 1982. Tetrachlorodibenzodioxin: A survey of subjects ten years after exposure. *British Journal of Industrial Medicine* 39:128-35.

96. Jennings, A.M., G. Wild, J.D. Ward, and A.M. Ward. 1988. Immunological abnormalities 17 years after accidental exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *British Journal of Industrial Medicine* 45:701-4.

97. Zober, A., M.G. Ott, and P. Messerer. 1994. Morbidity follow up study of BASF employees exposed to 2,3,7, 8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

98. Jansing, P.J., and R. Korff. 1994. Blood levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin and gamma-globulins in a follow-up investigation of employees with chloracne. *Journal of Dermatological Science* 8:91-5.

99. Ott, M.G., A. Zober, and C. Germann, C. 1994. Laboratory results for selected target organs in 138 individuals occupationally exposed to TCDD. *Chemosphere* 29:2423-37.

100. Von Benner, A., L. Edler, K. Mayer, and A. Zober. 1994. 'Dioxin' investigation program of the chemical industry professional organization. *Arbeitsmedizin Sozialmedizin Praventivmedizin* 29:11-6.

101. Neubert, R., L. Maskow, G. Triebig, H.C. Broding, U. Jacob-Muller, H. Helge, and D. Neubert. 2000. Chlorinated dibenzo-p-dioxins and dibenzofurans and the human immune system: 3. Plasma immunoglobulins and cytokines of workers with quantified moderately increased body burdens. *Life Sciences* 66:2123-42.

102. Ernst, M., D. Flesch-Janys, I. Morgenstern, and A. Manz. 1998. Immune cell functions in industrial workers after exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin: Dissociation of antigen-specific T-cell responses in cultures of diluted whole blood and of isolated peripheral blood mononuclear cells. *Environmental Health Perspectives* 106(Suppl 2):701-5.

103. Jung, D., P.A. Berg, L. Edler, W. Ehrenthal, D. Fenner, D. Flesch-Janys, C. Huber, R. Klein, C. Koitka, G. Lucier, A. Manz, A. Muttray, L. Needham, O. Papke, M. Pietsch, C. Portier, D. Patterson, W. Prellwitz, D.M. Rose, A. Thews, and J. Konietzko. 1998. Immunologic findings in workers formerly exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin and its congeners. *Environmental Health Perspectives* 106(Suppl 2):689-95.

104. Halperin, W., R. Vogt, M.H. Sweeney, G. Shopp, M. Fingerhut, and M. Petersen. 1998. Immunological markers among workers exposed to 2,3,7,8- tetrachlorodibenzo-p-dioxin. *Occupational and Environmental Medicine* 55:742-9.

105. Takata, T. 2003. Survey on the health effect of chronic exposure to dioxins and its accumulation on workers of a municipal solid waste incinerator, rural part of Osaka Prefecture, and the results of extended survey afterwards. *Industrial Health* 41:189-96.

106. Lathrop, G.D., W.H. Wolfe, R.A. Albanese, and P.M. Moynahan. 1984. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Baseline morbidity study results. NTIS: AD A 138 340. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

107. Lathrop, G.D., S.G. Machado, T.G. Karrison, W.D. Grubbs, W.F. Thomas, W.H. Wolfe, J.E. Michalek, J.C. Miner, and M.R. Peterson. 1987. Epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: First followup examination results. NTIS: AD A 188 262. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

108. Thomas, W.F., W.D. Grubbs, T.G. Karrison, M.B. Lustik, R.H. Roegner, D.E. Williams, W.H. Wolfe, J.E. Michalek, J.C. Miner, and R.W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

109. Roegner, R.H., W.D. Grubbs, M.B. Lustik, A.S. Brockman, S.C. Henderson, D.E. Williams, W.H. Wolfe, J.E. Michalek, and J.C. Miner. 1991. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Serum dioxin analysis of 1987 examination results. NTIS: AD A 237 516-24. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

110. Grubbs, W.D., W.H. Wolfe, J.E. Michalek, D.E. Williams, M.B. Lustik, A.S. Brockman, S.C. Henderson, F.R. Burnett, R.G. Land, D.J. Osborne, V.K. Rocconi, M.E. Schreiber, J.C. Miner, G.L. Henriksen, and J.A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1992 followup examination results. NTIS: AD A 304 306, 304 308-316. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

111. Michalek, J.E., B.R. Burnham, H.E. Marden, Jr., J.N. Robinson, V.V. Elequin, J.C. Miner, R.W. Ogershok, W.K. Sneddon, W.D. Grubbs, B.C. Cooper, R.G. Land, V.K. Rocconi, M.E. Yeager, D.E. Williams, and M.E.B. Owens. 2000. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1997 follow-up examination results. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

112. Michalek, J.E., N.S. Ketchum, and I.J. Check. 1999. Serum dioxin and immunologic response in veterans of Operation Ranch Hand. *American Journal of Epidemiology* 149:1038-46.

113. Kim, H.A., E.M. Kim, Y.C. Park, J.Y. Yu, S.K. Hong, S.H. Jeon, K.L. Park, S.J. Hur, and Y. Heo. 2003. Immunotoxicological effects of Agent Orange exposure to the Vietnam War Korean veterans. *Industrial Health* 41:158-66.

114. Institute of Medicine. 2003. Veterans and Agent Orange: Update 2002. National Academy Press: Washington, DC.

115. Garrow, J.S., and Webster, J. 1985. Quetelet's index (W/H^2) as a measure of fatness. *International Journal of Obesity* 9:147-53.

116. Piani, A., and C. Schoenborn. 1993. Health promotion and disease prevention: United States, 1990. National Center for Health Statistics. Vital Health Statistics Series No. 10 (185).

117. Stephens, T., and C.L. Craig. 1989. Fitness and activity measurement in the 1981 Canada Fitness Survey. In: National Center for Health Statistics. Assessing Physical Fitness and Physical Activity in Population-Based Surveys. T.F. Drury, ed. Public Health Service: Hyattsville, MD.

118. Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L.R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

119. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57:369-78.

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20 PULMONARY ASSESSMENT

20.1 INTRODUCTION

20.1.1 Background

20.1.1.1 Organs/Diseases

The Air Force Health Study (AFHS) included clinical assessments and questionnaire ascertainment of several nonmalignant respiratory outcomes, including asthma, bronchitis, pneumonia, and thorax and lung abnormality based on the presence of asymmetrical expansion, hyperresonance, dullness, wheezes, rales, or chronic obstructive pulmonary disease (COPD). The analyses of these outcomes in previous AFHS reports have adjusted for current and lifetime smoking. Mortality and morbidity studies evaluated the relation between dioxin exposure and these diverse nonmalignant acute and chronic respiratory diseases. Morbidity studies used the following clinical measures as study endpoints: lung or thorax abnormalities found on clinical examination; pulmonary function tests, such as forced expiratory volume at one second (FEV_1), which measures airflow obstruction, and forced vital capacity (FVC), which measures restriction; and abnormalities found on chest x-ray films.

Cigarette smoking is a strong risk factor for many respiratory diseases; consequently, smoking could easily obscure weaker associations between disease and other exposures, such as dioxin. Smoking history was often not available or considered in most studies that evaluated nonmalignant respiratory disease among dioxin exposed individuals, even though U.S. veterans reportedly smoked more heavily than nonveterans (1).

20.1.1.2 Toxicology

The toxic effects of dioxin most likely occur as a result of dioxin binding to a protein, the aryl hydrocarbon (Ah) receptor, which initiates a sequence of events at the cellular level, including the induction of enzymes capable of metabolizing chemicals to reactive intermediates (2, 3). Several studies have demonstrated that dioxin enhances the activity of cytochrome P-450 and Ah hydroxylase in respiratory tract epithelium. Research into the pulmonary toxicity of dioxin in laboratory animals has focused on the physiochemical properties of the Ah receptor and the carcinogenic potential of the cytochrome P-450 enzyme system in mice (4), rats (5, 6), and rabbits (7-12). A recent study found that gestational and lactational dioxin exposure to rats resulted in the induction of the cytochrome P-450 1A1 and 1A2 enzymes in the lungs of offspring that was long-lasting and gender-dependent (13). Both cytochrome P-450 enzymes have been found in human lung biopsy specimens (14).

In mice, the induction of cytochrome P-450 enzymes by dioxin in the lung was found similar to that in the liver (15). In rats (16, 17), the intratracheal administration of dioxin was associated with significant dose-related increases in hepatic enzymes as well, establishing the transpulmonary absorption of dioxin and the potential for pneumotoxicity. The most recent update of the Institute of Medicine's (IOM) *Veterans and Agent Orange* report states that it is biologically plausible that exposure to dioxin could be related to acute and chronic lung disease (18). Given that smoking is a major risk factor for these disorders and that the cytochrome P-450 enzymes also play a role in the activation of chemicals found in cigarette smoke, it is possible that dioxin may synergize the adverse effects of other chemicals (18).

20.1.1.3 Epidemiology

Early case reports of chemical workers exposed to dioxin-contaminated herbicides through industrial accidents have described acute respiratory effects, including irritation (19) and tracheo-bronchitis (20). The well-studied cohort that includes Seveso, Italy, residents exposed to substantial amounts of relatively pure dioxin following an industrial accident in 1976 is one of a few nonoccupationally exposed populations. The mortality experience of the cohort through 1991 (up to 15 years) (21, 22) was compared to a large population from the surrounding noncontaminated territory. Findings revealed that male residents closest to the plant at the time of the accident experienced a twofold increase in mortality from all respiratory diseases and a threefold increase for COPD mortality. The most recent update by Bertazzi and colleagues (23), which extended the follow-up to 20 years, reported results similar to earlier reports.

Studies of occupationally exposed workers revealed both nonmalignant respiratory morbidity and mortality. In one such study, workers exposed to dioxin had similar chest x-ray film findings when compared to unexposed referents. Although significant reductions were reported in FEV_1 and FVC among cigarette smokers only, pulmonary measures remained significantly reduced in the dioxin-exposed cohort relative to controls (24). Zober and colleagues (25) found that dioxin-exposed workers with severe chloracne had significantly more episodes of respiratory diseases overall, and specifically more upper respiratory tract infections and COPD than referents. In contrast, another occupational cohort did not exhibit increases in chronic bronchitis, COPD, or abnormal pulmonary function parameters, such as FEV_1 and FVC (26, 27).

Occupational mortality studies have generally demonstrated lower mortality rates for respiratory disease than expected (28-34). The largest of these, a multinational historical cohort study of 21,863 workers (32, 33), reported a statistically significant reduced rate (18%) of respiratory disease mortality for males based on 252 observed deaths. Few studies included dose of dioxin from biomonitoring data or estimated dose from job histories (31-34), and none adjusted their statistical analyses for the confounding effect of smoking.

No differences in chest x-ray film findings (35, 36) or pulmonary function tests have been found in studies of Vietnam veterans compared to non-Vietnam veterans (35). The frequency of self-reported physician-diagnosed chronic bronchitis was not significantly different between veterans who served in Southeast Asia (SEA) and veterans who served elsewhere (37). Furthermore, among those with service in SEA, the frequency of chronic bronchitis among herbicide handlers did not differ significantly from nonhandlers (37). Reports of other chronic respiratory conditions, including colds, hay fever, bronchitis, and emphysema, were higher among Australian Army Vietnam veterans compared to the general Australian population (38). Although results were not adjusted for smoking, the authors reported that the proportion of Vietnam veterans who had ever smoked was significantly higher than the proportion in the general population.

Similar to occupational studies, studies of the Air Force Ranch Hand cohort (39) reported that Vietnam veterans exhibited fewer deaths than the referent group for nonmalignant respiratory diseases, including one report of fewer than expected deaths from COPD, specifically (40). The mortality described by Dalager and Kang (41) of Army Chemical Corps veterans found a statistically nonsignificant excess of respiratory system diseases among Corps veterans who served in Vietnam compared to non-Vietnam veterans. Chemical Corps veterans were responsible for the storage, preparation, and applications of a variety of herbicides, including Agent Orange.

Overall, with the exception of the recent Seveso reports (21-23), mortality studies have failed to find any excess of respiratory disease mortality, and more often reported fewer deaths than expected. Many studies are hampered by one or more methodological limitations, including relatively few observed deaths, the absence of data on confounders such as smoking, and the reliance on death certificates for cause of death information. Furthermore, though a few of these studies assessed COPD mortality

separately, most grouped the wide range of respiratory disorders and assessed mortality for "all nonmalignant respiratory diseases" collectively.

In the 1987 and 1992 AFHS examinations, Ranch Hand participants were more likely than the Comparison group to have an abnormality of the thorax and lungs (42, 43); this finding was not seen in the 1997 examination (44). Ranch Hands and Comparisons did not differ on any respiratory measures in 1987, 1992, or 1997. In the analysis of the 1987 and 1992 follow-up examinations, a reduction in FVC, and as a consequence, an increase in the FEV_1 to FVC ratio, was noted in association with increasing serum dioxin levels. The 1997 examination also showed that Ranch Hands were more likely to have a history of bronchitis and asthma than the Comparison group. Ranch Hand officers exhibited a significantly higher prevalence of mild obstructive abnormality than the Comparison officers, which persisted after adjustment for smoking (44).

The IOM *Veterans and Agent Orange* reports, including the most recent 2002 update, consistently concluded that there is "inadequate or insufficient" evidence to determine the existence of an association between exposure to certain herbicides used in Vietnam and nonmalignant respiratory disorders (18).

20.1.2 Summary of Previous Analyses of the Air Force Health Study

20.1.2.1 1982 Baseline Examination Summary Results

The 1982 baseline examination explored a history of pulmonary disease by questionnaire and active pulmonary function by standardized spirometric techniques. These areas were of significant interest because of reported operational inhalation of Agent Orange by some Ranch Hand enlisted flyers and enlisted groundcrew.

The questionnaire revealed no group differences for historical diagnoses of tuberculosis and fungal infections, pneumonia, cancer, or chronic sinusitis and upper respiratory disease. At the physical examination, the Ranch Hand and Comparison unadjusted means for FEV_1 (percent predicted), FVC, and the ratio of FEV_1 to FVC were similar. Adjusted mean values were not calculated because of significant interactions (group-by-age for FEV_1 and FVC, group-by-smoking for the ratio of FEV_1 to FVC).

Exposure analyses showed two significant associations in the enlisted flyer and enlisted groundcrew strata, but neither was indicative of a linear dose-response relation. Overall, there were no pulmonary diseases, pulmonary function data, or associations of concern.

20.1.2.2 1985 Follow-up Examination Summary Results

Because of the lack of significant results from the pulmonary analyses from the baseline examination, pulmonary function (spirometric) studies were not performed during the 1985 follow-up examination. Collection of pulmonary data was limited to a questionnaire history of respiratory disease, physical examination of the thorax and lungs, and pulmonary abnormalities detected on a routine chest x-ray film. Mortality because of respiratory disease also was evaluated.

There were no significant group differences found for reported history of asthma, bronchitis, pleurisy, or tuberculosis based on the analyses adjusted for age and lifetime smoking, although there was a significant group-by-lifetime smoking interaction for pleurisy and tuberculosis. Ranch Hands who were moderate lifetime smokers (up to 10 pack-years) had a significantly increased prevalence of pleurisy and tuberculosis than did Comparisons who were moderate lifetime smokers.

Similarly, there were no significant group differences in the adjusted analyses for the radiological and clinical respiratory findings of thorax and lungs, asymmetrical expansion, hyperresonance, dullness, wheezes, rales, and the interpretation of the chest x-ray film. Also, the exposure index analyses revealed no consistent dose-response pattern.

20.1.2.3 1987 Follow-up Examination Summary Results

The pulmonary assessment was based on five self-reported respiratory illnesses, seven clinical observations, and eight laboratory measurements. The self-reported illnesses were based on participant-reported responses to the personal history form and the health history questionnaire and confirmed by medical records review. No evidence of a herbicide effect was detected in the assessment of the reported respiratory illnesses. No significant group differences were detected in the adjusted analyses when comparing all Ranch Hands with all Comparisons. Exploration of interactions did not reveal a consistent pattern indicating a herbicide effect. The adverse effects of smoking on pulmonary status were evident in all analyses.

20.1.2.4 Serum Dioxin Analysis of 1987 Follow-up Examination Summary Results

In general, there was no association between initial dioxin levels and the self-reported respiratory illnesses and clinical observations. For the majority of the laboratory measurements, there appeared to be an inverse association with initial dioxin. In the categorized dioxin analyses, the percentage of abnormalities did not differ significantly among the four dioxin categories for any of the questionnaire and physical examination variables, except under the analysis of an abnormality of the thorax and lung. In this case, Ranch Hands in the high dioxin category had a higher percentage of abnormalities than did Comparisons; but Ranch Hands in the low dioxin category had a lower percentage of abnormalities than did Comparisons. For the continuous variables, the means differed among the dioxin categories. For FVC, FEV_1, and forced expiratory flow maximum (FEFmax), the mean for the Ranch Hands in the unknown (termed as "background" in subsequent reports) category tended to be greater than the mean for the Comparisons in the background category, but the means for the low and high categories were less than the mean for the background category. In the analysis of the ratio of observed FEV_1 to observed FVC, this trend was reversed.

In the longitudinal analysis of the ratio of observed FEV_1 to observed FVC, there was a significant positive association with 1987 dioxin and a significant difference among the dioxin categories, with the mean increase from 1982 to 1987 in the high dioxin category greater than the mean increase from 1982 to 1987 in Comparisons.

In summary, the historical, physical examination, and most laboratory data analyzed from the 1987 follow-up examination for associations with serum dioxin revealed no evidence for an increased occurrence of pulmonary disease in the Ranch Hand cohort in relation to the body burden of dioxin. Analysis of two laboratory variables, FVC and the ratio of observed FEV_1 to observed FVC, yielded results that were consistent with subtle dose-response effects related to the body burden of dioxin in Ranch Hands.

20.1.2.5 1992 Follow-up Examination Summary Results

For the medical records and physical examination pulmonary variables, the group analysis revealed significant associations for bronchitis and thorax and lung abnormality. For enlisted flyers, significantly more Ranch Hands than Comparisons had bronchitis and a thorax and lung abnormality. The initial dioxin, categorized dioxin, and 1987 dioxin analyses for these variables did not confirm a dioxin dose-response relation.

For the laboratory variables, a statistically significant inverse relation was revealed between percent of predicted FVC and initial and 1987 dioxin for Ranch Hands. When Ranch Hands were contrasted with Comparisons, no significant differences were detected. Also, the analysis of the ratio of observed FEV_1 to observed FVC within Ranch Hands revealed a significant relation with initial dioxin indicating that the ratio increases (becomes closer to 1) for increasing levels of initial dioxin, which may have been due to the diminishing magnitude of FVC in the denominator of the ratio.

In the longitudinal analysis of the ratio of observed FEV_1 to observed FVC, there was a significant group difference for the enlisted flyers. The Ranch Hand enlisted flyers had a larger decrease in the ratio between 1982 and 1992 than did the Comparison enlisted flyers.

In summary, the historical, physical examination, and laboratory data analyzed for this assessment revealed no consistent evidence of an increased prevalence of pulmonary disease in the Ranch Hand cohort in relation to body burden of dioxin.

20.1.2.6 1997 Follow-up Examination Summary Results

To assess the pulmonary status for the 1997 AFHS follow-up examination, verified histories of asthma, bronchitis, and pneumonia were studied. A composite measure of thorax and lung abnormality, as determined from the presence of asymmetrical expansion, hyperresonance, dullness, wheezes, rales, COPD, or the physician's assessment of abnormality, also was analyzed. A routine chest x-ray film and five measures of pulmonary function using standard spirometric techniques were analyzed.

Few significant increases in adverse pulmonary conditions were observed for Ranch Hands, and isolated and inconsistent associations between the pulmonary endpoints and increased dioxin were seen. No consistent pattern or dose-response relation was evident. Ranch Hands in the background dioxin category exhibited a significantly higher percentage of abnormalities on the chest x-ray film than did Comparisons. Ranch Hand officers had a significantly higher prevalence of mild obstructive abnormality than did Comparison officers; the corresponding contrast was not significant in 1992, and officers were not analyzed as a separate stratum in 1982, 1985, or 1987. The meaning of this finding was unclear because the risk was not significantly increased in Ranch Hand enlisted groundcrew—the military occupation with the highest median dioxin level.

20.1.3 Parameters for the 2002 Pulmonary Assessment

20.1.3.1 Dependent Variables

The pulmonary assessment was based on questionnaire, physical examination, and laboratory data collected at the 2002 follow-up examination.

20.1.3.1.1 Medical Records Variables

In the self-administered family and personal history section, each study participant was asked whether he had ever experienced asthma, bronchitis, or pneumonia. The following International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes were used: asthma: 493.0–493.92; bronchitis: 466.0–466.19, 490.0–491.9, and 494.0-494.1; and pneumonia: 480.0–486 and 487.0. Medical records review was accomplished to confirm reported pulmonary conditions and to identify any unreported conditions for each participant that attended the 2002 physical examination. These data from the 2002 physical examination were combined with data from the 1982 baseline examination and the 1985, 1987, 1992, and 1997 follow-up examinations to form a complete history of asthma, bronchitis, and pneumonia for each participant. These three variables were individually analyzed as measures of the pulmonary health status of each participant. The analyses performed in this chapter were based on the 1,951 participants who attended the 2002 follow-up examination. Participants with occurrences of asthma, bronchitis, or pneumonia before duty in SEA were excluded from the analyses of the respective variables.

20.1.3.1.2 Physical Examination Variable

Part of the pulmonary assessment was based on the results of the physical examination of the thorax and lungs. A composite variable—thorax and lung abnormality—was constructed based on the presence or

absence of asymmetrical expansion, hyperresonance, dullness, wheezes, rales, or COPD, as well as the physician's assessment of abnormality. This variable was coded as "abnormal" if any of these conditions was present and "normal" if none of these conditions was present. No participants were excluded for medical reasons from the analysis of this variable.

20.1.3.1.3   Laboratory Variables

The assessment of the laboratory examination data included the interpretation of pulmonary abnormalities detected on a routine chest x-ray film. This variable was coded as "normal" or "abnormal." The assessment also included the analysis of pulmonary physiologic data collected during the physical examination employing standard spirometry techniques. Numerous indices were derived, including FVC—a measurement of the amount of air in liters expelled from maximum inspiration to full expiration—and FEV_1 in liters, an index derived from the FVC that quantifies the amount of air expelled at 1 second. The values used for these variables were the percentages of predicted values rather than the actual volume or flow rate. The calculations of the predicted values included an adjustment for age and height, as prescribed by the American Thoracic Society (ATS). The laboratory used the same predictive values regardless of race. For these indices, lower values indicated greater compromise in the lung function. These two variables were analyzed as continuous and discrete variables. In addition, the ratio of observed FEV_1 to observed FVC was calculated as an index reflective of obstructive airway disease. Lower values of this ratio also indicated greater compromise in the lung function.

As a guideline for determining normal and abnormal categories for percent of predicted FVC and FEV_1, the following ATS classifications for lung impairment were used (45):

- Normal function: >80%
- Mild impairment: 60–80%
- Moderate impairment: 50–59%
- Severe impairment: ≤49%.

Participants with mild, moderate, or severe impairment (≤80%) were classified as abnormal, and participants with normal lung function (>80%) were classified as normal. The FVC and the FEV_1 were based on the percent of predicted values, and the predicted values were adjusted for age and height.

Loss of vital capacity and obstructive abnormality were classified by the examiner as none, mild, moderate, or severe and analyzed as part of the pulmonary assessment. Due to the low frequencies in the moderate and severe categories, these two categories were combined in the analysis of loss of vital capacity.

Participants judged by the Scripps Clinic pulmonologist to have inadequate technical quality were excluded from the analysis of FVC, FEV_1, the ratio of observed FEV_1 to observed FVC, loss of vital capacity, and obstructive abnormality. A spirometry test was considered to be of inadequate technical quality if any of the following criteria applied:

- There was extreme variability between the trials (extreme was defined as greater than 10%).
- The participant could not or did not exhale for at least 6 seconds.
- The "peak flow" was disproportionately low when compared to the other tests (requiring visual inspection of the graph).

20.1.3.2   Covariates

The effects of age, race, military occupation, current cigarette smoking (cigarettes /day), lifetime cigarette smoking history (pack-years), body mass index (kg/m^2), and exposure to industrial chemicals (yes, no) were used in adjusted statistical analyses evaluating the pulmonary dependent variables.

Age, race, and military occupation were determined from military records. Body mass index was calculated as weight/(height)^2, where the weight was measured in kilograms and the height was measured in meters at the physical examination (46). For purposes of covariate associations for discrete dependent variables, body mass index was dichotomized as "not obese" ($\leq$30 kg/m^2) and "obese" (>30 kg/m^2).

Current cigarette smoking and lifetime cigarette smoking history were based on questionnaire data. For lifetime cigarette smoking history, the respondent's average smoking was estimated over his lifetime based on his responses to the 2002 questionnaire, with 1 pack-year defined as 365 packs of cigarettes smoked during a single year. The participant's lifetime exposure through 1997 to industrial chemicals was updated with information reported in the 2002 questionnaire.

Current cigarette smoking was used as a covariate for the physical examination and laboratory variables only. Lifetime cigarette smoking history was used to investigate the cumulative effects of cigarette smoking.

20.1.4 Statistical Methods

Table 20-1 summarizes the statistical analysis performed for the 2002 pulmonary assessment. The first part of this table lists the dependent variables analyzed, source of the data, form of the data, cutpoints, covariates, exclusions, and statistical methods. The second part of the table further describes the covariates. A covariate was used in its continuous form whenever possible for all adjusted analyses. If the covariate was inherently discrete (e.g., military occupation), or if a categorized form was needed to develop measures of association with the dependent variables, the covariate was categorized as shown in Table 20-1.

Table 20-1. Statistical Analysis for the Pulmonary Assessment

Dependent Variables

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Asthma	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Bronchitis	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Pneumonia	MR-V	D	Yes No	(1)	(a)	U:LR,CS A:LR
Thorax and Lung Abnormality	PE	D	Yes No	(2)	None	U:LR,CS A:LR
X-ray Interpretation	LAB	D	Abnormal Normal	(2)	None	U:LR,CS A:LR
FVC (percent of predicted)	LAB	C/D	Abnormal: $\leq$80 Normal: >80	(2)	(b)	U:LR,CS,GLM,TT A:LR,GLM
FEV$_1$ (percent of predicted)	LAB	C/D	Abnormal: $\leq$80 Normal: >80	(2)	(b)	U:LR,CS,GLM,TT A:LR,GLM
Ratio of Observed FEV$_1$ to Observed FVC	LAB	C	--	(2)	(b)	U:GLM,TT A:GLM
Loss of Vital Capacity	LAB	D	Moderate/Severe Mild None	(2)	(b)	U:PR,CS A:PR

Variable (Units)	Data Source	Data Form	Cutpoints	Covariates[a]	Exclusions[b]	Statistical Analysis and Methods
Obstructive Abnormality	LAB	D	Severe Moderate Mild None	(2)	(b)	U:PR,CS A:PR

[a]Covariates:

(1) age, race, military occupation, body mass index, lifetime cigarette smoking history, lifetime exposure to industrial chemicals.

(2) age, race, military occupation, body mass index, current cigarette smoking, lifetime cigarette smoking history, lifetime exposure to industrial chemicals.

[b]Exclusions:

(a) participants with a pre-SEA history of the disorder.

(b) participants judged to have inadequate technical quality on the 2002 AFHS follow-up examination spirometry examination.

Covariates

Variable (Units)	Data Source	Data Form	Cutpoints
Age (years)	MIL	C/D	Born ≥1942 Born <1942
Race	MIL	D	Black Non-Black
Military Occupation	MIL	D	Officer Enlisted Flyer Enlisted Groundcrew
Body Mass Index (kg/m^2)	PE	C/D	Not Obese: ≤30 Obese: >30
Current Cigarette Smoking (cigarettes/day)	Q-SR	C/D	Never Former >0–20 >20
Lifetime Cigarette Smoking History (pack-years)	Q-SR	C/D	0 >0–10 >10
Lifetime Exposure to Industrial Chemicals	Q-SR	D	Yes No

Abbreviations

Data Source:

LAB: 2002 laboratory results

MIL: Air Force military records

MR-V: Medical records (verified)

PE: 2002 physical examination

Q-SR: AFHS health questionnaires (self-reported)

Data Form:

C: Continuous form of dependent variable

D: Discrete form of dependent variable or covariate

C/D: Continuous and discrete forms of dependent variable; appropriate form for analysis (either continuous or discrete) of covariate

Statistical Analysis: U: Unadjusted analysis
                           A: Adjusted analysis

Statistical Methods: CS: Chi-square contingency table analysis (continuity-adjusted for 2x2 tables)
                           GLM: General linear models analysis
                           LR: Logistic regression analysis
                           PR: Polytomous logistic regression analysis
                           TT: Two-sample t-test

Four models were examined for each dependent variable given in Table 20-1. The analyses of these models are presented below. Further details on dioxin and the modeling strategy are found in Chapters 2 and 7, respectively. These analyses were performed both unadjusted and adjusted for covariates. These covariates are given in Table 20-1. Model 1 examined the relation between the dependent variable and group (i.e., Ranch Hand or Comparison). In this model, exposure was defined as "yes" for Ranch Hands and "no" for Comparisons without regard to the magnitude of the exposure. In an attempt to quantify exposure, three contrasts of Ranch Hands and Comparisons were performed along with the overall Ranch Hand versus Comparison contrast. These three contrasts compared Ranch Hands and Comparisons within each military occupational category (i.e., officers, enlisted flyers, and enlisted groundcrew). As described in previous reports and Table 2-4, the median level of exposure to dioxin was highest for enlisted groundcrew, followed by enlisted flyers, then officers.

During the 1987, 1992, 1997, and 2002 examinations, serum dioxin levels were measured by the Centers for Disease Control and Prevention (CDC) using high-resolution gas chromatography and high-resolution mass spectrometry and were reported in parts per trillion (ppt) on a lipid weight basis (47). These dioxin measurements are referred to as "lipid-adjusted." All measures of dioxin used in this report were based on lipid-adjusted dioxin measurements.

Model 2 examined the relation between the dependent variable and an extrapolated initial dioxin measure for Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt. The initial dioxin was calculated by extrapolating the 1987 dioxin level back in time to the end of the tour of duty that qualified a Ranch Hand veteran for inclusion in this study. If a Ranch Hand did not have a 1987 dioxin level, then the first dioxin measured, either at 1992, 1997, or 2002, was used to estimate the initial dioxin level. Regardless of when the dioxin was measured, Ranch Hand veterans with a level less than or equal to 10 ppt were excluded from statistical analyses based on Model 2. A statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model to account for body mass index-related differences in elimination rate (48).

Model 3 divided the Ranch Hands examined in Model 2 into two categories based on their initial dioxin measures. These two categories were referred to as "low Ranch Hand" and "high Ranch Hand." Two additional categories—Ranch Hands with serum dioxin levels at or below 10 ppt and Comparisons—were formed and included in the model. Ranch Hands with serum dioxin levels at or below 10 ppt were assigned to the "background Ranch Hand" category. If a Ranch Hand did not have a 1987 dioxin measurement, the first measured dioxin level was used. Another category was examined by combining the low and high Ranch Hand categories. This combination is referred to in the tables as the "low plus high Ranch Hand" category. These five categories—Comparisons, background Ranch Hands, low Ranch Hands, high Ranch Hands, and low plus high Ranch Hands—were used in Model 3 analyses. The relation between the dependent variable in each of the four Ranch Hand categories and the dependent variable in the Comparison category was examined. As in Model 2, a statistical adjustment for body mass index at the time of the participant's blood measurement of dioxin was included in this model for the

unadjusted and adjusted analyses of all dependent variables. One Ranch Hand without a dioxin measure was excluded from statistical analyses based on Model 3.

Model 4 examined the relation between the dependent variable and 1987 dioxin levels in all Ranch Hands with a dioxin measurement. If a Ranch Hand did not have a 1987 dioxin measurement, the first dioxin level obtained, either in 1992, 1997, or 2002, was extrapolated to the date of the 1987 physical examination. If the first dioxin level was not obtained in 1987 and was less than or equal to 10 ppt, it was not extrapolated to 1987 level, but was used at the measured value. One Ranch Hand without a dioxin measurement was excluded from statistical analyses based on Model 4.

The term "unadjusted" was used in the text and tables as follows: Models 1 and 4 did not adjust for any covariates. Models 2 and 3 adjusted only for body mass index at the time of the blood measurement for dioxin. The term "adjusted" was used in the text and tables as follows: Models 1 and 4 adjusted for the covariates shown in Table 20-1 unless otherwise specified by a footnote to the table. Models 2 and 3 additionally adjusted only for body mass index at the time of the blood measurement for dioxin.

Table 20-2 provides a summary of the number of participants with missing dependent variable and covariate data. In addition, the number of participants that were excluded from analyses is given.

Table 20-2. Number of Participants Excluded or with Missing Data for the Pulmonary Assessment

Variable	Variable Use	Group[a]		Dioxin (Ranch Hands Only)[b]		Categorized Dioxin[c]	
		Ranch Hand	Comparison	Initial Dioxin	1987 Dioxin	Ranch Hand	Comparison
Thorax and Lung Abnormality	DEP	1	0	0	1	1	0
X-ray Interpretation	DEP	3	0	1	3	3	0
FVC	DEP	8	11	4	8	8	11
FEV_1	DEP	8	11	4	8	8	11
Ratio of Observed FEV_1 to Observed FVC	DEP	8	11	4	8	8	11
Loss of Vital Capacity	DEP	12	15	6	12	12	15
Obstructive Abnormality	DEP	12	16	7	12	12	16
Lifetime Cigarette Smoking History	COV	0	3	0	0	0	3
Current Cigarette Smoking	COV	0	2	0	0	0	2
Body Mass Index	COV	1	0	0	1	1	0
Pre-SEA Asthma	EXC	9	6	6	9	9	6
Pre-SEA Bronchitis	EXC	21	23	12	21	21	23
Pre-SEA Pneumonia	EXC	40	41	21	40	40	41
Inadequate Technical Quality	EXC	1	2	1	1	1	2

[a]777 Ranch Hands and 1,174 Comparisons for group.
[b]424 Ranch Hands for initial dioxin; 776 Ranch Hands for 1987 dioxin.
[c]776 Ranch Hands and 1,174 Comparisons for categorized dioxin.

Note: DEP = Dependent variable.
       COV = Covariate.
       EXC = Exclusion.

20.2 RESULTS

20.2.1 Dependent Variable-covariate Associations

The pulmonary dependent variables were tested for associations with each of the covariates used in the adjusted analyses. The complete results are presented in Appendix F, Table F-12. These associations were pairwise between the dependent variable and the covariate and were not adjusted for any other covariates. A brief summary of the pattern of significant ($p \leq 0.05$) dependent variable-covariate associations is described in the following paragraphs. In the discussion of the results below, low levels were considered adverse for FVC and FEV_1.

As age increased, the number of abnormalities for asthma, bronchitis, pneumonia, thorax and lungs, x-ray interpretation, and FEV_1 increased. As age increased, FEV_1 and the ratio of observed FEV_1 to observed FVC decreased. More obstructive abnormality and moderate or severe loss of vital capacity were observed in the older participants, but more mild loss of vital capacity was seen in the younger participants.

As expected, a lower mean FVC and FEV_1 were seen in Blacks, as well as an increased number of abnormally low measurements. The ratio of observed FEV_1 to observed FVC was lower in non-Blacks because the difference between Blacks and non-Blacks in FVC was larger than the difference in FEV_1 between Blacks and non-Blacks. Loss of vital capacity was higher among Black participants, but the presence of an obstructive abnormality was more prevalent among non-Black participants.

Thorax and lung abnormalities were more prevalent among enlisted flyers. Mean FVC levels were lower for enlisted personnel than for officers, and the percentage of abnormally low FVC measurements was higher for enlisted personnel than officers. Mean FEV_1 levels were lowest for enlisted flyers, and the percentage of abnormally low FEV_1 measurements was highest for enlisted flyers. The ratio of observed FEV_1 to observed FVC was lower for officers and enlisted flyers than for enlisted groundcrew. Mild loss of vital capacity was more prevalent among enlisted personnel than officers. Obstructive abnormalities were also more prevalent among enlisted flyers, followed by officers, then enlisted groundcrew.

The percentage of thorax and lung abnormalities and abnormal x-ray interpretations increased as the number of cigarettes per day currently smoked increased. Former and moderate current cigarette smokers (no more than one pack a day, on average) exhibited the higher percentages of FVC abnormalities and loss of vital capacity. FEV_1 and the ratio of observed FEV_1 to FVC decreased as current cigarette smoking increased. The percentage of abnormally low FEV_1 also increased as current cigarette smoking increased. A higher prevalence of and more severe obstructive abnormalities were seen as current cigarette smoking increased.

Bronchitis, thorax and lung abnormalities, and abnormal x-ray interpretations were more prevalent in the heaviest smokers. FVC and FEV_1 decreased as lifetime cigarette smoking history increased, as did the ratio of observed FEV_1 to observed FVC. The prevalence of abnormally low FVC and FEV_1 values increased as lifetime cigarette smoking history increased. A higher prevalence of and more severe loss of vital capacity and obstructive abnormality were seen as lifetime cigarette smoking history increased.

As body mass index increased, FVC and FEV_1 decreased. An increased number of abnormally low measurements was seen for FVC and FEV_1 in obese participants. As body mass index decreased, the ratio of observed FEV_1 to observed FVC decreased because the association between body mass index and FVC was stronger than the association between body mass index and FEV_1. Mild, moderate, or severe loss of vital capacity was observed more often in obese participants. Mild and severe obstructive abnormalities were less prevalent in obese participants, but moderate obstructive abnormalities were more prevalent in obese participants.

More thorax and lung abnormalities and low FVC measurements were observed in participants who had been exposed to industrial chemicals than in those who had not been exposed to industrial chemicals.

20.2.2 Exposure Analysis

The following section presents results of the statistical analyses of the dependent variables shown in Table 20-1. Dependent variables are grouped into three sections: (1) medical records variables, derived from the questionnaire that was administered in the 2002 follow-up and previous AFHS examinations and verified by a review of medical records, (2) variables obtained during the 2002 physical examination, and (3) pulmonary laboratory variables.

20.2.2.1 Medical Records Variables

20.2.2.1.1   Asthma

All unadjusted and adjusted results from the analyses of a history of asthma were nonsignificant for Models 1 through 4 (Table 20-3(a-h): $p>0.11$ for each analysis).

Table 20-3. Analysis of Asthma

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*50 (6.5)*	*1.01 (0.70,1.47)*	*0.938*
	Comparison	*1,168*	*75 (6.4)*		
Officer	Ranch Hand	304	21 (6.9)	1.10 (0.62,1.97)	0.741
	Comparison	460	29 (6.3)		
Enlisted Flyer	Ranch Hand	131	5 (3.8)	0.45 (0.16,1.27)	0.131
	Comparison	185	15 (8.1)		
Enlisted Groundcrew	Ranch Hand	333	24 (7.2)	1.23 (0.71,2.14)	0.457
	Comparison	523	31 (5.9)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,932*	*1.01 (0.70,1.46)*	*0.959*
Officer	763	1.09 (0.61,1.96)	0.761
Enlisted Flyer	316	0.43 (0.15,1.23)	0.115
Enlisted Groundcrew	853	1.24 (0.72,2.16)	0.440

Table 20-3. Analysis of Asthma (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for $\log_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	136	8 (5.9)	0.99 (0.72,1.37)	0.964
Medium	143	7 (4.9)		
High	139	8 (5.8)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for $\log_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
418	0.88 (0.60,1.28)	0.491

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,168	75 (6.4)		
Background RH	349	27 (7.7)	1.25 (0.79,1.99)	0.335
Low RH	207	12 (5.8)	0.89 (0.47,1.67)	0.715
High RH	211	11 (5.2)	0.78 (0.41,1.50)	0.462
Low plus High RH	418	23 (5.5)	0.83 (0.51,1.35)	0.461

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 20-3. Analysis of Asthma (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,165		
Background RH	348	1.27 (0.80,2.04)	0.311
Low RH	207	0.87 (0.46,1.64)	0.670
High RH	211	0.76 (0.39,1.49)	0.427
Low plus High RH	418	0.81 (0.50,1.33)	0.411

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	258	15 (5.8)	0.92 (0.77,1.10)	0.362
Medium	253	20 (7.9)		
High	256	15 (5.9)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
766	0.88 (0.71,1.08)	0.225

[a]Relative risk for a twofold increase in 1987 dioxin.

20.2.2.1.2   Bronchitis

All Models 1 through 4 results from the unadjusted and adjusted analyses of a history of bronchitis were nonsignificant (Table 20-4(a-h): p>0.12 for each analysis).

Table 20-4. Analysis of Bronchitis

(a) MODEL 1: RANCH HANDS VS. COMPARISONS − UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*756*	*242 (32.0)*	*1.07 (0.88,1.30)*	*0.510*
	Comparison	*1,151*	*352 (30.6)*		
Officer	Ranch Hand	296	89 (30.1)	0.97 (0.70,1.33)	0.842
	Comparison	452	139 (30.8)		
Enlisted Flyer	Ranch Hand	127	47 (37.0)	1.46 (0.90,2.36)	0.126
	Comparison	181	52 (28.7)		
Enlisted Groundcrew	Ranch Hand	333	106 (31.8)	1.04 (0.77,1.39)	0.818
	Comparison	518	161 (31.1)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,903*	*1.06 (0.86,1.29)*	*0.596*
Officer	747	0.96 (0.69,1.32)	0.792
Enlisted Flyer	308	1.45 (0.89,2.37)	0.135
Enlisted Groundcrew	848	1.02 (0.76,1.38)	0.900

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	133	47 (35.3)	1.01 (0.86,1.18)	0.907
Medium	142	42 (29.6)		
High	137	44 (32.1)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
412	1.07 (0.89,1.28)	0.500

[a]Relative risk for a twofold increase in initial dioxin.

Table 20-4. Analysis of Bronchitis (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,151	352 (30.6)		
Background RH	343	108 (31.5)	1.07 (0.82,1.39)	0.629
Low RH	203	67 (33.0)	1.11 (0.81,1.53)	0.513
High RH	209	66 (31.6)	1.03 (0.75,1.41)	0.870
Low plus High RH	412	133 (32.3)	1.07 (0.84,1.36)	0.594

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,148		
Background RH	342	1.06 (0.81,1.39)	0.647
Low RH	203	1.05 (0.76,1.45)	0.773
High RH	209	1.01 (0.73,1.41)	0.933
Low plus High RH	412	1.03 (0.80,1.32)	0.808

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	254	79 (31.1)	1.00 (0.91,1.10)	0.973
Medium	248	82 (33.1)		
High	253	80 (31.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 20-4. Analysis of Bronchitis (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

| | Analysis Results for Log$_2$ (1987 Dioxin) | |
| | Adjusted Relative Risk | |
n	(95% C.I.)[a]	p-Value
754	0.99 (0.88,1.11)	0.851

[a]Relative risk for a twofold increase in 1987 dioxin.

20.2.2.1.3   Pneumonia

Both the unadjusted and adjusted Model 1 analyses of a history of pneumonia displayed a significant difference between Ranch Hands and Comparisons within the enlisted flyer stratum (Table 20-5(a,b): Unadjusted Relative Risk [RR]=1.91, p=0.049; and Adjusted RR=1.94, p=0.046). A total of 19.7 percent of Ranch Hand enlisted flyers exhibited a history of pneumonia compared to 11.4 percent of Comparison enlisted flyers. All other Model 1 contrasts and all unadjusted and adjusted results from Models 2 through 4 were each nonsignificant (Table 20-5(a-h): p>0.09 for all remaining analyses).

Table 20-5. Analysis of Pneumonia

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*737*	*97 (13.2)*	*0.92 (0.70,1.20)*	*0.520*
	Comparison	*1,133*	*161 (14.2)*		
Officer	Ranch Hand	290	39 (13.4)	0.87 (0.57,1.33)	0.512
	Comparison	441	67 (15.2)		
Enlisted Flyer	Ranch Hand	122	24 (19.7)	1.91 (1.00,3.64)	0.049*
	Comparison	176	20 (11.4)		
Enlisted Groundcrew	Ranch Hand	325	34 (10.5)	0.70 (0.45,1.08)	0.103
	Comparison	516	74 (14.3)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,866*	*0.91 (0.69,1.20)*	*0.509*
Officer	730	0.87 (0.57,1.34)	0.535
Enlisted Flyer	298	1.94 (1.01,3.72)	0.046*
Enlisted Groundcrew	838	0.69 (0.45,1.06)	0.093

*: Statistically significant (0.010<p-value≤0.050).

Table 20-5. Analysis of Pneumonia (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	**n**	**Number (%) Yes**	**Unadjusted Relative Risk (95% C.I.)[a,b]**	**p-Value**
Low	128	22 (17.2)	0.84 (0.67,1.06)	0.125
Medium	139	16 (11.5)		
High	136	16 (11.8)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	**Adjusted Relative Risk (95% C.I.)[a]**	**p-Value**
403	0.85 (0.65,1.12)	0.243

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,133	161 (14.2)		
Background RH	333	43 (12.9)	0.92 (0.64,1.32)	0.654
Low RH	195	31 (15.9)	1.13 (0.74,1.72)	0.569
High RH	208	23 (11.1)	0.73 (0.46,1.17)	0.189
Low plus High RH	403	54 (13.4)	0.90 (0.64,1.26)	0.551

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 20-5. Analysis of Pneumonia (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,130		
Background RH	332	0.90 (0.62,1.31)	0.586
Low RH	195	1.07 (0.70,1.64)	0.749
High RH	208	0.79 (0.49,1.27)	0.325
Low plus High RH	403	0.91 (0.65,1.29)	0.602

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	242	29 (12.0)	0.95 (0.83,1.08)	0.436
Medium	243	39 (16.0)		
High	251	29 (11.6)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log_2 (1987 Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
735	0.94 (0.79,1.10)	0.433

[a]Relative risk for a twofold increase in 1987 dioxin.

20.2.2.2 Physical Examination Variable

20.2.2.2.1 Thorax and Lung Abnormality

The Model 1 unadjusted analysis of thorax and lung abnormality revealed a significant difference between Ranch Hands and Comparisons when examined across all occupations and within the enlisted flyer stratum (Table 20-6(a): Unadjusted RR=1.28, p=0.039; and Unadjusted RR=1.68, p=0.041 for all participants and for enlisted flyers, respectively). Each significant result was nonsignificant after adjusting for covariates (Table 20-6(b): p=0.226 and p=0.141 for all participants and for enlisted flyers,

respectively). All other Model 1 unadjusted and adjusted contrasts and each result from the analyses of Model 2 were nonsignificant (Table 20-6(a-d): p>0.19 for each result).

A significant difference between Ranch Hands in the low and high dioxin categories combined and Comparisons was revealed within the unadjusted Model 3 analysis of thorax and lung abnormality (Table 20-6(e): Unadjusted RR=1.37, p=0.025). The difference was nonsignificant after adjusting for covariates (Table 12-6(f): p=0.479). All other Model 3 unadjusted and adjusted contrasts, as well as each result from Model 4, were nonsignificant (Table 20-6(e-h): p>0.07 for each analysis).

Table 20-6. Analysis of Thorax and Lung Abnormality

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*776*	*159 (20.5)*	*1.28 (1.01,1.61)*	*0.039**
	Comparison	*1,174*	*197 (16.8)*		
Officer	Ranch Hand	306	38 (12.4)	1.07 (0.69,1.67)	0.760
	Comparison	462	54 (11.7)		
Enlisted Flyer	Ranch Hand	133	44 (33.1)	1.68 (1.02,2.77)	0.041*
	Comparison	185	42 (22.7)		
Enlisted Groundcrew	Ranch Hand	337	77 (22.8)	1.25 (0.89,1.74)	0.192
	Comparison	527	101 (19.2)		

*: Statistically significant (0.010<p-value≤0.050).

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,947*	*1.18 (0.90,1.54)*	*0.226*
Officer	768	1.07 (0.67,1.70)	0.793
Enlisted Flyer	318	1.55 (0.87,2.77)	0.141
Enlisted Groundcrew	861	1.12 (0.76,1.66)	0.569

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	22 (15.7)	1.04 (0.88,1.24)	0.645
Medium	143	40 (28.0)		
High	141	29 (20.6)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

Table 20-6. Analysis of Thorax and Lung Abnormality (Continued)

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
424	0.94 (0.74,1.18)	0.587

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	197 (16.8)		
Background RH	351	67 (19.1)	1.14 (0.84,1.56)	0.401
Low RH	211	45 (21.3)	1.35 (0.94,1.95)	0.103
High RH	213	46 (21.6)	1.40 (0.97,2.01)	0.071
Low plus High RH	424	91 (21.5)	1.37 (1.04,1.82)	0.025*

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.010 < $p-value$ \leq 0.050$).

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,171		
Background RH	351	1.27 (0.88,1.82)	0.197
Low RH	211	1.20 (0.79,1.82)	0.395
High RH	213	1.06 (0.68,1.64)	0.808
Low plus High RH	424	1.12 (0.81,1.56)	0.479

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 20-6. Analysis of Thorax and Lung Abnormality (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Yes	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	259	48 (18.5)	1.02 (0.92,1.14)	0.658
Medium	258	46 (17.8)		
High	258	64 (24.8)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
	Adjusted Relative Risk	
n	(95% C.I.)[a]	p-Value
775	0.93 (0.80,1.07)	0.315

[a]Relative risk for a twofold increase in 1987 dioxin.

20.2.2.3 Laboratory Examination Variables

20.2.2.3.1 X-ray Interpretation

The Model 2 unadjusted analysis of the x-ray interpretation revealed a significant inverse association between initial dioxin and the x-ray interpretation (Table 20-7(c): Unadjusted RR=0.80, p=0.040). After adjusting for covariates, however, the association was nonsignificant (Table 20-7(d): p=0.117). All other results of the unadjusted and adjusted analyses of the x-ray interpretation were nonsignificant for Models 1, 3, and 4 (Table 20-7(a,b,e-h): p>0.09 for each analysis).

Table 20-7. Analysis of X-ray Interpretation

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*774*	*119 (15.4)*	*0.86 (0.67,1.10)*	*0.224*
	Comparison	*1,174*	*205 (17.5)*		
Officer	Ranch Hand	305	43 (14.1)	0.77 (0.52,1.15)	0.207
	Comparison	462	81 (17.5)		
Enlisted Flyer	Ranch Hand	133	27 (20.3)	1.17 (0.67,2.07)	0.580
	Comparison	185	33 (17.8)		
Enlisted Groundcrew	Ranch Hand	336	49 (14.6)	0.82 (0.56,1.19)	0.297
	Comparison	527	91 (17.3)		

Table 20-7. Analysis of X-ray Interpretation (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,945*	*0.84 (0.65,1.07)*	*0.160*
Officer	767	0.76 (0.51,1.14)	0.192
Enlisted Flyer	318	1.13 (0.64,2.00)	0.679
Enlisted Groundcrew	860	0.80 (0.54,1.17)	0.246

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	140	28 (20.0)	0.80 (0.64,1.00)	0.040*
Medium	142	23 (16.2)		
High	141	14 (9.9)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

	Analysis Results for Log_2 (Initial Dioxin)	
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
423	0.82 (0.64,1.06)	0.117

[a]Relative risk for a twofold increase in initial dioxin.

Table 20-7. Analysis of X-ray Interpretation (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,174	205 (17.5)		
Background RH	350	53 (15.1)	0.84 (0.61,1.17)	0.312
Low RH	211	38 (18.0)	1.04 (0.71,1.52)	0.847
High RH	212	27 (12.7)	0.69 (0.45,1.06)	0.093
Low plus High RH	423	65 (15.4)	0.85 (0.62,1.15)	0.288

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,171		
Background RH	350	0.83 (0.59,1.17)	0.296
Low RH	211	0.94 (0.64,1.39)	0.769
High RH	212	0.69 (0.44,1.09)	0.110
Low plus High RH	423	0.81 (0.59,1.11)	0.188

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	258	42 (16.3)	0.93 (0.82,1.05)	0.239
Medium	258	40 (15.5)		
High	257	36 (14.0)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

Table 20-7. Analysis of X-ray Interpretation (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)	
	Adjusted Relative Risk	
n	**(95% C.I.)[a]**	**p-Value**
773	0.91 (0.78,1.05)	0.184

[a]Relative risk for a twofold increase in 1987 dioxin.

20.2.2.3.2 FVC (Continuous)

Results from the unadjusted and adjusted analyses of the continuous form of FVC were nonsignificant for Models 1 and 2 (Table 20-8(a-d): p>0.29 for each analysis).

The Model 3 unadjusted analysis of the continuous form of FVC displayed significant differences in means between Ranch Hands in the low dioxin category and Comparisons and between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 20-8(e): difference of adjusted means=-3.86 percent, p=0.001; and difference of adjusted means=-2.58 percent, p=0.005, respectively). In the adjusted analysis, the contrast between Ranch Hands in the low dioxin category and Comparisons remained significant (Table 20-8(f): difference of adjusted means=-2.52 percent, p=0.031), while the contrast between Ranch Hands in the low and high dioxin categories combined and Comparisons became nonsignificant (Table 20-8(f): p=0.052). Ranch Hands in the low dioxin category had a lower adjusted mean FVC (93.22 percent) than Comparisons (95.74 percent). All other Model 3 contrasts, both unadjusted and adjusted, were nonsignificant (Table 20-8(f): p>0.26 for all remaining contrasts).

A significant inverse association between FVC and 1987 dioxin levels was found in the Model 4 unadjusted analysis (Table 20-8(g): Slope=-1.419, p<0.001). After adjusting for covariates, the association was nonsignificant (Table 20-8(h): p=0.109).

Table 20-8. Analysis of FVC (percent of predicted) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*100.84*	*-0.81 (-2.32,0.70)*	*0.293*
	Comparison	*1,161*	*101.65*		
Officer	Ranch Hand	304	103.34	-0.26 (-2.65,2.13)	0.830
	Comparison	459	103.60		
Enlisted Flyer	Ranch Hand	130	99.18	-1.69 (-5.40,2.02)	0.372
	Comparison	183	100.87		
Enlisted Groundcrew	Ranch Hand	334	99.21	-0.99 (-3.26,1.28)	0.393
	Comparison	519	100.20		

Table 20-8. Analysis of FVC (percent of predicted) (Continuous) (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*94.93*	*-0.74 (-2.14,0.67)*	*0.303*
	Comparison	*1,159*	*95.67*		
Officer	Ranch Hand	304	96.12	-0.08 (-2.31,2.15)	0.945
	Comparison	459	96.20		
Enlisted Flyer	Ranch Hand	130	94.12	-1.83 (-5.30,1.64)	0.301
	Comparison	183	95.95		
Enlisted Groundcrew	Ranch Hand	334	94.17	-0.93 (-3.05,1.19)	0.390
	Comparison	517	95.10		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	138	98.07	97.80	0.034	0.269 (0.543)	0.621
Medium	140	98.01	97.95			
High	141	99.08	99.41			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	138	93.86	0.136	-0.631 (0.607)	0.299
Medium	140	93.10			
High	141	93.12			

Table 20-8. Analysis of FVC (percent of predicted) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,161	101.65	101.72		
Background RH	348	103.82	102.68	0.95 (-0.98,2.89)	0.334
Low RH	207	97.51	97.86	-3.86 (-6.23,-1.49)	0.001**
High RH	212	99.25	100.39	-1.33 (-3.69,1.03)	0.269
Low plus High RH	419	98.39	99.14	-2.58 (-4.37,-0.78)	0.005**

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
　　　 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,159	95.74		
Background RH	348	96.17	0.44 (-1.45,2.32)	0.651
Low RH	207	93.22	-2.52 (-4.81,-0.23)	0.031*
High RH	212	94.78	-0.96 (-3.30,1.38)	0.420
Low plus High RH	419	94.01	-1.73 (-3.48,0.02)	0.052

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
　　　 Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
　　　 Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
　　　 High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log_2 (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean	R^2	Slope (Standard Error)	p-Value
Low	257	105.52	0.020	-1.419 (0.356)	<0.001**
Medium	253	98.32			
High	257	98.67			

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

Table 20-8.   Analysis of FVC (percent of predicted) (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	257	97.38	0.166	-0.631 (0.393)	0.109
Medium	253	93.23			
High	257	94.07			

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

20.2.2.3.3   FVC (Discrete)

All results from the unadjusted and adjusted analyses of the discrete form of FVC were nonsignificant for Models 1 through 4 (Table 20-9(a-h): p>0.11 for each analysis).

Table 20-9. Analysis of FVC (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*71 (9.2)*	*0.92 (0.67,1.25)*	*0.587*
	Comparison	*1,161*	*116 (10.0)*		
Officer	Ranch Hand	304	22 (7.2)	1.01 (0.58,1.76)	0.980
	Comparison	459	33 (7.2)		
Enlisted Flyer	Ranch Hand	130	14 (10.8)	0.80 (0.40,1.61)	0.532
	Comparison	183	24 (13.1)		
Enlisted Groundcrew	Ranch Hand	334	35 (10.5)	0.91 (0.59,1.42)	0.686
	Comparison	519	59 (11.4)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,927*	*0.91 (0.66,1.26)*	*0.566*
Officer	763	0.99 (0.56,1.76)	0.986
Enlisted Flyer	313	0.75 (0.37,1.56)	0.448
Enlisted Groundcrew	851	0.93 (0.58,1.48)	0.751

Table 20-9. Analysis of FVC (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	20 (14.5)	0.82 (0.64,1.05)	0.112
Medium	140	15 (10.7)		
High	141	9 (6.4)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
419	0.88 (0.66,1.18)	0.386

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,161	116 (10.0)		
Background RH	348	27 (7.8)	0.87 (0.56,1.36)	0.545
Low RH	207	27 (13.0)	1.30 (0.83,2.05)	0.255
High RH	212	17 (8.0)	0.68 (0.40,1.17)	0.168
Low plus High RH	419	44 (10.5)	0.94 (0.64,1.37)	0.749

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
     Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
     Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
     High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 20-9. Analysis of FVC (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,159		
Background RH	348	0.98 (0.62,1.56)	0.946
Low RH	207	1.10 (0.68,1.77)	0.702
High RH	212	0.67 (0.38,1.17)	0.160
Low plus High RH	419	0.85 (0.58,1.27)	0.433

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	16 (6.2)	1.03 (0.89,1.20)	0.673
Medium	253	34 (13.4)		
High	257	21 (8.2)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
767	0.93 (0.77,1.12)	0.452

[a]Relative risk for a twofold increase in 1987 dioxin.

20.2.2.3.4   *FEV$_1$ (Continuous)*

The Model 3 unadjusted analysis of the continuous form of FEV$_1$ revealed significant differences in adjusted means between Ranch Hands in the low dioxin category and Comparisons and between Ranch Hands in the low and high dioxin categories combined and Comparisons (Table 20-10(e): difference of adjusted means=-4.11 percent, p=0.002; and difference of adjusted means=-2.12 percent, p=0.033, respectively). Both results became nonsignificant after adjusting for covariates (Table 20-10(f): p=0.064 and p=0.203, respectively). All other Model 3 results, as well as all other results from the unadjusted and adjusted analyses of FEV$_1$ from Models 1, 2, and 4, were each nonsignificant (Table 20-10(a-h): p>0.12 for each analysis result).

Table 20-10. Analysis of FEV$_1$ (percent of predicted) (Continuous)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean	Difference of Unadjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*88.18*	*-1.22 (-2.81,0.38)*	*0.136*
	Comparison	*1,161*	*89.40*		
Officer	Ranch Hand	304	89.72	-1.48 (-4.00,1.05)	0.252
	Comparison	459	91.20		
Enlisted Flyer	Ranch Hand	130	84.49	-1.87 (-5.79,2.04)	0.349
	Comparison	183	86.37		
Enlisted Groundcrew	Ranch Hand	334	88.21	-0.66 (-3.05,1.74)	0.591
	Comparison	519	88.87		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean	Difference of Adjusted Means (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*84.44*	*-0.84 (-2.32,0.65)*	*0.270*
	Comparison	*1,159*	*85.28*		
Officer	Ranch Hand	304	85.20	-1.29 (-3.65,1.06)	0.283
	Comparison	459	86.49		
Enlisted Flyer	Ranch Hand	130	83.36	-1.35 (-5.01,2.31)	0.469
	Comparison	183	84.71		
Enlisted Groundcrew	Ranch Hand	334	84.57	-0.23 (-2.47,2.01)	0.840
	Comparison	517	84.80		

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean	Adjusted Mean[a]	R^2	Slope (Standard Error)[a]	p-Value
Low	138	85.83	85.79	0.006	0.929 (0.602)	0.124
Medium	140	85.36	85.35			
High	141	89.91	89.97			

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean	R^2	Adjusted Slope (Standard Error)	p-Value
Low	138	84.37	0.155	0.028 (0.655)	0.966
Medium	140	83.79			
High	141	85.96			

Table 20-10. Analysis of FEV₁ (percent of predicted) (Continuous) (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons (95% C.I.)[a]	p-Value
Comparison	1,161	89.40	89.42		
Background RH	348	89.62	89.24	-0.18 (-2.28,1.92)	0.869
Low RH	207	85.19	85.31	-4.11 (-6.69,-1.53)	0.002**
High RH	212	88.86	89.24	-0.18 (-2.74,2.38)	0.890
Low plus High RH	419	87.05	87.30	-2.12 (-4.07,-0.17)	0.033*

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.

  *: Statistically significant (0.010<p-value≤0.050).
**: Statistically significant (p-value≤0.010).

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
Comparison	1,159	85.33		
Background RH	348	85.09	-0.23 (-2.22,1.76)	0.818
Low RH	207	83.04	-2.29 (-4.71,0.13)	0.064
High RH	212	85.19	-0.14 (-2.60,2.33)	0.915
Low plus High RH	419	84.13	-1.20 (-3.04,0.65)	0.203

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log₂ (1987 Dioxin)		
1987 Dioxin	n	Unadjusted Mean	R^2	Slope (Standard Error)	p-Value
Low	257	91.33	0.001	-0.287 (0.386)	0.457
Medium	253	85.69			
High	257	87.59			

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

Table 20-10. Analysis of FEV₁ (percent of predicted) (Continuous) (Continued)

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log₂ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean**	**R^2**	**Adjusted Slope (Standard Error)**	**p-Value**
Low	257	86.91	0.170	-0.169 (0.421)	0.688
Medium	253	83.25			
High	257	84.19			

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

20.2.2.3.5   FEV₁ (Discrete)

A significant difference between Ranch Hands in the low dioxin category and Comparisons was found within the unadjusted Model 3 analysis of the discrete form of FEV₁ (Table 20-11(e): Unadjusted RR=1.39, p=0.039). After adjusting for covariates, the difference was nonsignificant (Table 20-11(f): p=0.390). Similar to the analysis of the continuous form of FEV₁, all other Model 3 contrasts, as well as all contrasts from Models 1, 2 and 4, were each nonsignificant from the unadjusted and adjusted analyses of the discrete form of FEV₁ (Table 20-11(a-h): p>0.22 for each result).

Table 20-11. Analysis of FEV₁ (Discrete)

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*768*	*241 (31.4)*	*1.10 (0.90,1.34)*	*0.347*
	Comparison	*1,161*	*341 (29.4)*		
Officer	Ranch Hand	304	88 (28.9)	1.14 (0.82,1.57)	0.433
	Comparison	459	121 (26.4)		
Enlisted Flyer	Ranch Hand	130	56 (43.1)	1.28 (0.81,2.02)	0.292
	Comparison	183	68 (37.2)		
Enlisted Groundcrew	Ranch Hand	334	97 (29.0)	0.99 (0.73,1.34)	0.939
	Comparison	519	152 (29.3)		

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,927*	*1.06 (0.86,1.31)*	*0.564*
Officer	763	1.14 (0.81,1.60)	0.445
Enlisted Flyer	313	1.24 (0.76,2.02)	0.393
Enlisted Groundcrew	851	0.94 (0.68,1.29)	0.687

Table 20-11. Analysis of FEV₁ (Discrete) (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log_2 (Initial Dioxin)	
Initial Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	138	48 (34.8)	0.91 (0.78,1.06)	0.227
Medium	140	54 (38.6)		
High	141	35 (24.8)		

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Analysis Results for Log_2 (Initial Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
419	1.00 (0.82,1.21)	0.981

[a]Relative risk for a twofold increase in initial dioxin.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison	1,161	341 (29.4)		
Background RH	348	103 (29.6)	1.04 (0.80,1.36)	0.769
Low RH	207	76 (36.7)	1.39 (1.02,1.89)	0.039*
High RH	212	61 (28.8)	0.95 (0.68,1.31)	0.742
Low plus High RH	419	137 (32.7)	1.14 (0.90,1.46)	0.278

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant ($0.010<\text{p-value}\leq0.050$).

Note: RH = Ranch Hand.
      Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
      Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
      High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 20-11. Analysis of FEV$_1$ (Discrete) (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,159		
Background RH	348	1.04 (0.78,1.38)	0.795
Low RH	207	1.16 (0.83,1.61)	0.390
High RH	212	0.95 (0.67,1.36)	0.794
Low plus High RH	419	1.05 (0.81,1.36)	0.720

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)	
1987 Dioxin	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	257	66 (25.7)	1.02 (0.93,1.12)	0.697
Medium	253	94 (37.2)		
High	257	80 (31.1)		

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

Analysis Results for Log$_2$ (1987 Dioxin)		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
767	1.03 (0.91,1.16)	0.677

[a]Relative risk for a twofold increase in 1987 dioxin.

20.2.2.3.6 *Ratio of Observed FEV$_1$ to Observed FVC*

All Model 1 unadjusted and adjusted analyses of the ratio of observed FEV$_1$ to observed FVC were nonsignificant (Table 20-12(a,b): p>0.07 for each contrast).

Both the unadjusted and adjusted Model 2 analyses of the ratio of observed FEV$_1$ to observed FVC displayed significant results (Table 20-12(c,d): Slope=-0.032, p=0.004; and Adjusted Slope=-0.023, p=0.039, respectively). Because of the transformation used, this result indicated that the ratio of observed FEV$_1$ to observed FVC increased as initial dioxin increased. The adjusted mean ratio of observed FEV$_1$ to observed FVC was 0.729 for the low initial dioxin category, 0.740 for the medium initial dioxin

category, and 0.752 for the high initial dioxin category. A significant difference of means between Ranch Hands in the high dioxin category and Comparisons was found within the Model 3 unadjusted analysis of the ratio of observed FEV_1 to observed FVC (Table 20-12(e): difference of adjusted means=0.013, p=0.027). After adjusting for covariates, the difference became nonsignificant (Table 20-12(f): p=0.220). All other unadjusted and adjusted Model 3 contrasts were also nonsignificant (Table 20-12(e,f): p>0.05 for each remaining contrast).

The unadjusted Model 4 analysis of the ratio of observed FEV_1 to observed FVC was significant (Table 20-12(g): Slope=-0.031, p<0.001). After adjusting for covariates, however, the association was nonsignificant (Table 20-12(h): p=0.083).

Table 20-12. Analysis of Ratio of Observed FEV_1 to Observed FVC

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Unadjusted Mean[a]	Difference of Unadjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*0.713*	*-0.004*	*0.358*
	Comparison	*1,161*	*0.717*		
Officer	Ranch Hand	304	0.701	-0.011	0.091
	Comparison	459	0.712		
Enlisted Flyer	Ranch Hand	130	0.700	0.002	0.825
	Comparison	183	0.697		
Enlisted Groundcrew	Ranch Hand	334	0.729	0.001	0.836
	Comparison	519	0.728		

[a]Transformed from natural logarithm scale of 1.0 - ratio.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 - ratio.
[c]P-value was based on difference of means on natural logarithm scale of 1.0 - ratio.

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	Group	n	Adjusted Mean[a]	Difference of Adjusted Means[b]	p-Value[c]
All	*Ranch Hand*	*768*	*0.726*	*-0.001*	*0.698*
	Comparison	*1,159*	*0.727*		
Officer	Ranch Hand	304	0.720	-0.010	0.074
	Comparison	459	0.730		
Enlisted Flyer	Ranch Hand	130	0.727	0.007	0.414
	Comparison	183	0.720		
Enlisted Groundcrew	Ranch Hand	334	0.733	0.003	0.537
	Comparison	517	0.730		

[a]Transformed from natural logarithm scale of 1.0 - ratio.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 - ratio.
[c]P-value was based on difference of means on natural logarithm scale of 1.0 - ratio.

Table 20-12. Analysis of Ratio of Observed FEV$_1$ to Observed FVC (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

Initial Dioxin Category Summary Statistics				Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	R^2	Slope (Standard Error)[b,c]	p-Value
Low	138	0.706	0.707	0.043	-0.032 (0.011)	0.004**
Medium	140	0.718	0.718			
High	141	0.741	0.740			

[a]Transformed from natural logarithm scale of 1.0 - ratio.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Slope and standard error based on natural logarithm of 1.0 - ratio versus log$_2$ (initial dioxin); because of this transformation, a negative slope implies a positive association between the ratio and log$_2$ (initial dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

Initial Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (Initial Dioxin)		
Initial Dioxin	n	Adjusted Mean[a]	R^2	Adjusted Slope (Standard Error)[b]	p-Value
Low	138	0.729	0.246	-0.023 (0.011)	0.039*
Medium	140	0.740			
High	141	0.752			

[a]Transformed from natural logarithm scale of 1.0 - ratio.
[b]Slope and standard error based on natural logarithm of 1.0 - ratio versus log$_2$ (initial dioxin); because of this transformation, a negative slope implies a positive association between the ratio and log$_2$ (initial dioxin).

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Unadjusted Mean[a]	Adjusted Mean[a,b]	Difference of Adjusted Mean vs. Comparisons[b,c]	p-Value[d]
Comparison	1,161	0.717	0.717		
Background RH	348	0.703	0.707	-0.010	0.056
Low RH	207	0.710	0.709	-0.008	0.201
High RH	212	0.734	0.730	0.013	0.027*
Low plus High RH	419	0.722	0.720	0.003	0.528

[a]Transformed from natural logarithm scale of 1.0 - ratio.
[b]Adjusted for body mass index at the time of the blood measurement of dioxin.
[c]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 - ratio.
[d]P-value was based on difference of means on natural logarithm scale of 1.0 - ratio.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Adjusted Mean[a]	Difference of Adjusted Mean vs. Comparisons[b]	p-Value[c]
Comparison	1,159	0.727		
Background RH	348	0.723	-0.004	0.325
Low RH	207	0.725	-0.002	0.683
High RH	212	0.734	0.007	0.220
Low plus High RH	419	0.730	0.003	0.572

[a]Transformed from natural logarithm scale of 1.0 - ratio.
[b]Difference of means after transformation to original scale; confidence interval on difference of means not presented because analysis was performed on natural logarithm scale of 1.0 - ratio.
[c]P-value was based on difference of means on natural logarithm scale of 1.0 - ratio.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 20-12. Analysis of Ratio of Observed FEV₁ to Observed FVC (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log₂ (1987 Dioxin)		
1987 Dioxin	**n**	**Unadjusted Mean[a]**	**R^2**	**Slope (Standard Error)[b]**	**p-Value**
Low	257	0.704	0.028	-0.031 (0.007)	<0.001**
Medium	253	0.707			
High	257	0.729			

[a]Transformed from natural logarithm scale of 1.0 - ratio.
[b]Slope and standard error based on natural logarithm of 1.0 - ratio versus log₂ (1987 dioxin); because of this transformation, a negative slope implies a positive association between the ratio and log₂ (1987 dioxin).

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

1987 Dioxin Category Summary Statistics			Analysis Results for Log₂ (1987 Dioxin)		
1987 Dioxin	**n**	**Adjusted Mean[a]**	**R^2**	**Adjusted Slope (Standard Error)[b]**	**p-Value**
Low	257	0.729	0.238	-0.012 (0.007)	0.083
Medium	253	0.727			
High	257	0.734			

[a]Transformed from natural logarithm scale of 1.0 - ratio.
[b]Slope and standard error based on natural logarithm of 1.0 - ratio versus log₂ (1987 dioxin); because of this transformation, a negative slope implies a positive association between the ratio and log₂ (1987 dioxin).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

20.2.2.3.7   Loss of Vital Capacity

All results from the unadjusted and adjusted analyses of loss of vital capacity from Models 1, 2, and 4 were nonsignificant, both unadjusted and adjusted for covariates (Table 20-13(a-d,g,h): p>0.12 for each contrast).

The unadjusted Model 3 analysis showed significantly more Comparisons than Ranch Hands in the background dioxin category with a mild loss of vital capacity (Table 20-13(e): Unadjusted RR=0.47, p=0.027). After adjusting for covariate effects, however, the contrast was nonsignificant (Table 20-13(f): p=0.075), as were all other unadjusted and adjusted Model 3 contrasts (Table 20-13(e-h): p>0.14 for each remaining contrast).

Table 20-13. Analysis of Loss of Vital Capacity

(a) MODEL 1: RANCH HANDS VS. COMPARISONS – UNADJUSTED

Occupational Category	Group	n	Number (%)			Mild vs. None		Moderate or Severe vs. None	
			None	Mild	Moderate or Severe	Unadjusted Relative Risk (95% C.I.)	p-Value	Unadjusted Relative Risk (95% C.I.)	p-Value
All	*Ranch Hand*	*765*	*713 (93.2)*	*38 (5.0)*	*14 (1.8)*	*0.73 (0.49,1.09)*	*0.126*	*0.86 (0.44,1.68)*	*0.669*
	Comparison	*1,158*	*1,057 (91.3)*	*77 (6.6)*	*24 (2.1)*				
Officer	Ranch Hand	304	288 (94.7)	10 (3.3)	6 (2.0)	0.79 (0.36,1.72)	0.553	1.12 (0.39,3.28)	0.829
	Comparison	459	432 (94.1)	19 (4.1)	8 (1.7)				
Enlisted Flyer	Ranch Hand	129	119 (92.2)	9 (7.0)	1 (0.8)	0.71 (0.31,1.65)	0.429	0.27 (0.03,2.33)	0.233
	Comparison	182	160 (87.9)	17 (9.3)	5 (2.7)				
Enlisted Groundcrew	Ranch Hand	332	306 (92.2)	19 (5.7)	7 (2.1)	0.70 (0.40,1.24)	0.222	0.97 (0.37,2.52)	0.945
	Comparison	517	465 (89.9)	41 (7.9)	11 (2.1)				

(b) MODEL 1: RANCH HANDS VS. COMPARISONS – ADJUSTED

Occupational Category	n	Mild vs. None		Moderate or Severe vs. None	
		Adjusted Relative Risk (95% C.I.)	p-Value	Adjusted Relative Risk (95% C.I.)	p-Value
All	*1,921*	*0.72 (0.48,1.09)*	*0.125*	*0.84 (0.42,1.66)*	*0.612*
Officer	763	0.77 (0.35,1.69)	0.514	1.14 (0.39,3.40)	0.809
Enlisted Flyer	311	0.68 (0.29,1.61)	0.379	0.25 (0.03,2.20)	0.211
Enlisted Groundcrew	847	0.72 (0.40,1.29)	0.264	0.92 (0.34,2.49)	0.866

Table 20-13. Analysis of Loss of Vital Capacity (Continued)

(c) MODEL 2: RANCH HANDS – INITIAL DIOXIN – UNADJUSTED

| Initial Dioxin Category | n | Initial Dioxin Category Summary Statistics Number (%) | | | Analysis Results for Log$_2$ (Initial Dioxin)[a] | | | |
| | | | | | Mild vs. None | | Moderate or Severe vs. None | |
		None	Mild	Moderate or Severe	Unadjusted Relative Risk (95% C.I.)[b]	p-Value	Unadjusted Relative Risk (95% C.I.)[b]	p-Value
Low	137	121 (88.3)	10 (7.3)	6 (4.4)	0.84 (0.62,1.14)	0.260	0.70 (0.39,1.28)	0.250
Medium	140	126 (90.0)	14 (10.0)	0 (0.0)				
High	140	134 (95.7)	4 (2.9)	2 (1.4)				

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS – INITIAL DIOXIN – ADJUSTED

| n | Analysis Results for Log$_2$ (Initial Dioxin) | | | |
| | Mild vs. None | | Moderate or Severe vs. None | |
	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	0.84 (0.60,1.17)	0.298	0.86 (0.43,1.70)	0.661

[a]Relative risk for a twofold increase in initial dioxin.

Note: Results were not adjusted for race and current cigarette smoking because of the sparse number of Ranch Hands with moderate or severe loss of vital capacity.

Table 20-13. Analysis of Loss of Vital Capacity (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – UNADJUSTED

Dioxin Category	n	Number (%) None	Number (%) Mild	Number (%) Moderate or Severe	Mild vs. None Unadjusted Relative Risk (95% C.I.)[a,b]	Mild vs. None p-Value	Moderate or Severe vs. None Unadjusted Relative Risk (95% C.I.)[a,b]	Moderate or Severe vs. None p-Value
Comparison	1,158	1,057 (91.3)	77 (6.6)	24 (2.1)				
Background RH	347	331 (95.4)	10 (2.9)	6 (1.7)	0.47 (0.24,0.92)	0.027*	1.02 (0.41,2.54)	0.974
Low RH	206	184 (89.3)	16 (7.8)	6 (2.9)	1.16 (0.66,2.04)	0.607	1.29 (0.51,3.28)	0.593
High RH	211	197 (93.4)	12 (5.7)	2 (0.9)	0.74 (0.39,1.40)	0.353	0.33 (0.08,1.47)	0.146
Low plus High RH	417	381 (91.4)	28 (6.7)	8 (1.9)	0.92 (0.59,1.46)	0.735	0.65 (0.26,1.65)	0.366

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

*: Statistically significant (0.010<p-value≤0.050).

Note: RH = Ranch Hand.   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY – ADJUSTED

Dioxin Category	n	Mild vs. None Adjusted Relative Risk (95% C.I.)[a]	Mild vs. None p-Value	Moderate or Severe vs. None Adjusted Relative Risk (95% C.I.)[a]	Moderate or Severe vs. None p-Value
Comparison	1,156				
Background RH	347	0.53 (0.27,1.07)	0.075	1.15 (0.45,2.96)	0.766
Low RH	206	0.95 (0.53,1.71)	0.870	1.06 (0.40,2.82)	0.904
High RH	211	0.68 (0.35,1.32)	0.251	0.40 (0.09,1.79)	0.231
Low plus High RH	417	0.80 (0.50,1.29)	0.362	0.65 (0.25,1.67)	0.369

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
       Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 20-13. Analysis of Loss of Vital Capacity (Continued)

(g) MODEL 4: RANCH HANDS – 1987 DIOXIN – UNADJUSTED

1987 Dioxin Category	n	1987 Dioxin Category Summary Statistics			Analysis Results for Log$_2$ (1987 Dioxin)[a]			
		Number (%)			Mild vs. None		Moderate or Severe vs. None	
		None	Mild	Moderate or Severe	Unadjusted Relative Risk (95% C.I.)[a]	p-Value	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	246 (96.1)	7 (2.7)	3 (1.2)	1.14 (0.94,1.39)	0.181	0.97 (0.70,1.35)	0.871
Medium	252	227 (90.1)	16 (6.3)	9 (3.6)				
High	256	239 (93.4)	15 (5.9)	2 (0.8)				

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Low = ≤7.8 ppt; Medium = >7.8-19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS – 1987 DIOXIN – ADJUSTED

	Analysis Results for Log$_2$ (1987 Dioxin)				
	Mild vs. None		Moderate or Severe vs. None		
n	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value	
764	1.05 (0.82,1.35)	0.683	0.85 (0.57,1.28)	0.447	

[a]Relative risk for a twofold increase in 1987 dioxin.

20.2.2.3.8   Obstructive Abnormality

The Model 1 adjusted analysis showed fewer Ranch Hands than Comparisons with a mild obstructive abnormality within the enlisted flyer stratum (Table 20-14(b): Adjusted RR=0.59, p=0.046). Ranch Hand enlisted flyers had fewer mild obstructive abnormalities (34.1%) than Comparison enlisted flyers (43.1%). All other Model 1 unadjusted and adjusted contrasts were nonsignificant (Table 20-14(a,b): p>0.08 for each remaining contrast).

Each contrast examined in the unadjusted Model 2 analysis displayed an inverse significant association between initial dioxin and obstructive abnormality (Table 20-14(c): mild vs. none, Unadjusted RR=0.82, p=0.019; moderate vs. none, Unadjusted RR=0.67, p=0.016; and severe vs. none, Unadjusted RR=0.50, p=0.022). Each of these results indicated a decrease in obstructive abnormality as initial dioxin increased. In the adjusted analysis the contrasts of moderate and severe obstructive abnormality remained significant (Table 20-14(d): Adjusted RR=0.64, p=0.023; and Adjusted RR=0.44, p=0.036, respectively). The mild obstructive abnormality contrast became nonsignificant in the adjusted analysis (Table 20-14(d): p=0.470). More Ranch Hands in the low dioxin category had moderate (11.7%) or severe obstructive abnormalities (4.4%) than Ranch Hands in the medium dioxin category (8.6% and 4.3% for moderate and severe obstructive abnormalities, respectively) or Ranch Hands in the high dioxin category (2.9% and 0.0% for moderate and severe obstructive abnormalities, respectively).

All Model 3 contrasts examined in both the unadjusted and adjusted analyses of obstructive abnormality were nonsignificant (Table 20-14(e, f): p>0.05 for each contrast).

An inverse significant association between obstructive abnormality and 1987 dioxin levels was seen in the Model 4 unadjusted analysis when a mild occurrence of obstructive abnormality was contrasted with no obstructive abnormality (Table 20-14(g): Unadjusted RR=0.88, p=0.009). The association became nonsignificant after adjusting for covariate effects (Table 20-14(h): p=0.901). All other Model 4 unadjusted and adjusted contrasts were nonsignificant (Table 20-14(g,h): p≥0.07).

Table 20-14. Analysis of Obstructive Abnormality

(a) MODEL 1: RANCH HANDS VS. COMPARISONS — UNADJUSTED									
Occupational Category	**Group**	**n**	**Number (%)**				**Contrast**	**Unadjusted Relative Risk (95% C.I.)**	**p-Value**
			None	**Mild**	**Moderate**	**Severe**			
All	*Ranch Hand*	*765*	*404 (52.8)*	*282 (36.9)*	*56 (7.3)*	*23 (3.0)*	*Mild vs. None*	*1.08 (0.88,1.31)*	*0.464*
	Comparison	*1,157*	*626 (54.1)*	*406 (35.1)*	*93 (8.0)*	*32 (2.8)*	*Moderate vs. None*	*0.93 (0.65,1.33)*	*0.701*
							Severe vs. None	*1.11 (0.64,1.93)*	*0.701*
Officer	Ranch Hand	304	140 (46.1)	133 (43.8)	21 (6.9)	10 (3.3)	Mild vs. None	1.18 (0.87,1.60)	0.282
	Comparison	459	234 (51.0)	188 (41.0)	26 (5.7)	11 (2.4)	Moderate vs. None	1.35 (0.73,2.49)	0.336
							Severe vs. None	1.52 (0.63,3.67)	0.352
Enlisted Flyer	Ranch Hand	129	64 (49.6)	44 (34.1)	15 (11.6)	6 (4.7)	Mild vs. None	0.64 (0.39,1.06)	0.083
	Comparison	181	73 (40.3)	78 (43.1)	23 (12.7)	7 (3.9)	Moderate vs. None	0.74 (0.36,1.55)	0.428
							Severe vs. None	0.98 (0.31,3.06)	0.969
Enlisted Groundcrew	Ranch Hand	332	200 (60.2)	105 (31.6)	20 (6.0)	7 (2.1)	Mild vs. None	1.20 (0.88,1.63)	0.255
	Comparison	517	319 (61.7)	140 (27.1)	44 (8.5)	14 (2.7)	Moderate vs. None	0.73 (0.42,1.27)	0.258
							Severe vs. None	0.80 (0.32,2.01)	0.631

Table 20-14. Analysis of Obstructive Abnormality (Continued)

(b) MODEL 1: RANCH HANDS VS. COMPARISONS — ADJUSTED				
Occupational Category	**n**	**Contrast**	**Adjusted Relative Risk (95% C.I.)**	**p-Value**
All	*1,920*	*Mild vs. None*	*1.03 (0.84,1.27)*	*0.748*
		Moderate vs. None	*0.86 (0.60,1.25)*	*0.436*
		Severe vs. None	*1.03 (0.58,1.84)*	*0.915*
Officer	763	Mild vs. None	1.17 (0.86,1.60)	0.324
		Moderate vs. None	1.34 (0.72,2.50)	0.362
		Severe vs. None	1.70 (0.68,4.23)	0.252
Enlisted Flyer	310	Mild vs. None	0.59 (0.35,0.99)	0.046*
		Moderate vs. None	0.63 (0.29,1.37)	0.246
		Severe vs. None	0.71 (0.21,2.37)	0.577
Enlisted Groundcrew	847	Mild vs. None	1.15 (0.83,1.59)	0.413
		Moderate vs. None	0.65 (0.36,1.18)	0.158
		Severe vs. None	0.70 (0.26,1.83)	0.463

*: Statistically significant (0.010<p-value≤0.050).

Table 20-14. Analysis of Obstructive Abnormality (Continued)

(c) MODEL 2: RANCH HANDS — INITIAL DIOXIN — UNADJUSTED

Initial Dioxin Category	Initial Dioxin Category Summary Statistics					Analysis Results for Log$_2$ (Initial Dioxin)		
		Number (%)						
	n	None	Mild	Moderate	Severe	Contrast	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Low	137	58 (42.3)	57 (41.6)	16 (11.7)	6 (4.4)	Mild vs. None	0.82 (0.70,0.97)	0.019*
Medium	140	78 (55.7)	44 (31.4)	12 (8.6)	6 (4.3)	Moderate vs. None	0.67 (0.49,0.93)	0.016*
High	140	95 (67.9)	41 (29.3)	4 (2.9)	0 (0.0)	Severe vs. None	0.50 (0.28,0.91)	0.022*

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt.

(d) MODEL 2: RANCH HANDS — INITIAL DIOXIN — ADJUSTED

		Analysis Results for Log$_2$ (Initial Dioxin)	
n	Contrast	Adjusted Relative Risk (95% C.I.)[a]	p-Value
417	Mild vs. None	0.93 (0.77,1.13)	0.470
	Moderate vs. None	0.64 (0.43,0.94)	0.023*
	Severe vs. None	0.44 (0.20,0.95)	0.036*

[a]Relative risk for a twofold increase in initial dioxin.

*: Statistically significant (0.010<p-value≤0.050).

Note: Results were not adjusted for race because of the sparse number of Black Ranch Hands with severe obstructive abnormality.

Table 20-14. Analysis of Obstructive Abnormality (Continued)

(e) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY — UNADJUSTED

Dioxin Category	n	Number (%)			
		None	Mild	Moderate	Severe
Comparison	1,157	626 (54.1)	406 (35.1)	93 (8.0)	32 (2.8)
Background RH	347	173 (49.9)	140 (40.4)	23 (6.6)	11 (3.2)
Low RH	206	95 (46.1)	81 (39.3)	20 (9.7)	10 (4.9)
High RH	211	136 (64.5)	61 (28.9)	12 (5.7)	2 (1.0)
Low plus High RH	417	231 (55.4)	142 (34.1)	32 (7.7)	12 (2.9)

Dioxin Category	Mild vs. None		Moderate vs. None		Severe vs. None	
	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value
Comparison						
Background RH	1.15 (0.89,1.49)	0.289	0.90 (0.55,1.47)	0.671	1.24 (0.61,2.52)	0.557
Low RH	1.34 (0.97,1.86)	0.076	1.41 (0.83,2.40)	0.199	2.06 (0.98,4.33)	0.056
High RH	0.74 (0.53,1.03)	0.073	0.59 (0.31,1.11)	0.103	0.29 (0.07,1.22)	0.092
Low plus High RH	0.99 (0.77,1.27)	0.953	0.91 (0.59,1.41)	0.675	0.76 (0.32,1.79)	0.535

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
  Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
  Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
  High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 20-14. Analysis of Obstructive Abnormality (Continued)

(f) MODEL 3: RANCH HANDS VS. COMPARISONS BY DIOXIN CATEGORY — ADJUSTED

Dioxin Category	n	Mild vs. None		Moderate vs. None		Severe vs. None	
		Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value	Adjusted Relative Risk (95% C.I.)[a]	p-Value
Comparison	1,155						
Background RH	347	1.00 (0.76,1.31)	0.993	0.85 (0.51,1.43)	0.541	1.16 (0.55,2.47)	0.692
Low RH	206	1.21 (0.86,1.69)	0.282	1.12 (0.64,1.96)	0.691	1.71 (0.77,3.77)	0.184
High RH	211	0.89 (0.62,1.28)	0.525	0.57 (0.29,1.12)	0.102	0.27 (0.06,1.18)	0.082
Low plus High RH	417	1.03 (0.79,1.35)	0.810	0.80 (0.50,1.27)	0.339	0.67 (0.27,1.62)	0.372

[a]Relative risk and confidence interval relative to Comparisons.

Note: RH = Ranch Hand.
    Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table 20-14. Analysis of Obstructive Abnormality (Continued)

(g) MODEL 4: RANCH HANDS — 1987 DIOXIN — UNADJUSTED

| | 1987 Dioxin Category Summary Statistics | | | | | Analysis Results for Log$_2$ (1987 Dioxin) | | |
| | | Number (%) | | | | | | |
1987 Dioxin Category	n	None	Mild	Moderate	Severe	Contrast	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
Low	256	136 (53.1)	99 (38.7)	13 (5.1)	8 (3.1)	Mild vs. None	0.88 (0.80,0.97)	0.009**
Medium	252	108 (42.9)	109 (43.3)	26 (10.3)	9 (3.6)	Moderate vs. None	0.93 (0.78,1.11)	0.433
High	256	160 (62.5)	74 (28.9)	16 (6.3)	6 (2.3)	Severe vs. None	0.78 (0.59,1.02)	0.070

[a]Relative risk for a twofold increase in 1987 dioxin.

**: Statistically significant (p-value≤0.010).

Note: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt.

(h) MODEL 4: RANCH HANDS — 1987 DIOXIN — ADJUSTED

| | | Analysis Results for Log$_2$ (1987 Dioxin) | |
n	Contrast	Adjusted Relative Risk (95% C.I.)[a]	p-Value
764	Mild vs. None	0.99 (0.88,1.12)	0.901
	Moderate vs. None	0.99 (0.80,1.24)	0.960
	Severe vs. None	0.79 (0.57,1.11)	0.177

[a]Relative risk for a twofold increase in 1987 dioxin.

Note: Results were not adjusted for race because of the sparse number of Black Ranch Hands with severe obstructive abnormality.

20.3 DISCUSSION

The AFHS assessed respiratory health by investigating the occurrence of asthma, bronchitis, and pneumonia, and the presence of an abnormality on physical examination of the thorax and lungs and as seen on a chest x-ray film. The pulmonary assessment also investigated lung function as measured by FVC, FEV_1, the FEV_1 to FVC ratio, and the severity of obstructive abnormality and loss of vital capacity. The criteria for an abnormal physical exam—any extraneous sound or percussion abnormality—may have led to the classification of more participants as abnormal than those who truly have chronic lung disease. Therefore, verified pulmonary diseases, radiographic abnormality, or spirometric abnormality may be more useful as a measure of compromised lung function than of abnormality on the physical examination. Respiratory endpoints were adjusted for the covariates of age, race, military occupation, body mass index, current and lifetime smoking history, and exposure to industrial chemicals.

Tests of association were performed between the dependent variable and each of the covariates used in the adjusted analyses. Many of the associations observed in the AFHS were consistent with patterns seen in clinical practice in pulmonary medicine. Age was associated with most of the respiratory endpoints. As expected, bronchitis, pneumonia, thorax or lung abnormalities, and radiographic abnormalities were all more prevalent in older participants. The decreased FEV_1 and FEV_1 to FVC ratio that was observed in older participants was consistent with published data and the known biologic loss of FEV_1 with increasing age (49). As expected, race was significantly associated with pulmonary function. FVC and FEV_1 were lower among Blacks compared to non-Blacks. Current smoking history and lifetime smoking history were associated with greater thorax and lung abnormalities, radiographic abnormalities, loss of vital capacity, loss of FEV_1, and obstructive abnormality. The associations observed in univariate analyses may be influenced by associations with other covariates, particularly smoking history.

The 2002 pulmonary assessment found no association between herbicide or dioxin exposure and asthma. This was consistent with prior follow-up examinations in which no differences in the prevalence of asthma between Ranch Hands and Comparisons have been seen.

The association between herbicide or dioxin exposure and the occurrence of respiratory infections was sporadic and inconsistent. The 2002 assessment found an increased history of pneumonia between Ranch Hand enlisted flyers compared with Comparison enlisted flyers; however, no dose-response effect was observed because there was no increased occurrence among enlisted groundcrew, who had the highest median dioxin level, and other models of dioxin exposure did not show a positive dose-response. The difference in the history of pneumonia between Ranch Hand and Comparison enlisted flyers also was observed during the 1992 physical examination, but was not significant in other AFHS examinations.

No differences in thorax and lung abnormalities on the physical examination or on an inspection of the chest x-ray film were found between Ranch Hands and Comparisons. Ranch Hands were more likely to have thorax and lung abnormalities in the 1987 and 1992 AFHS follow-up examinations, but no difference was observed in the 1997 and 2002 examinations. Chest x-ray abnormalities did not differ in any of the AFHS examinations.

In the 2002 examination, some differences in pulmonary function were observed. A statistically significant decrease in FVC was observed in the Ranch Hands in the low dioxin category relative to the Comparisons (93.22 percent vs. 95.74 percent). There was no clear dose response, because Ranch Hands in the high dioxin category had higher mean FVC levels than Ranch Hands in the low dioxin category. No significant differences in FVC were observed in the other models. No difference in FEV_1 was observed in any of the analyses. The ratio of FEV_1 to FVC increased among Ranch Hands as the initial dioxin level increased and the 1987 dioxin level increased. None of these statistically significant

differences in pulmonary function were clinically significant and the results of the ratio of FEV_1 to FVC analyses do not indicate an adverse dose-response effect.

No positive dose response relation was observed in the development of an obstructive abnormality between Ranch Hands and Comparisons. In fact, Ranch Hand enlisted flyers were less likely to have a mild obstructive abnormality than Comparison enlisted flyers. In addition, the percentage of participants with moderate and severe obstruction decreased as initial dioxin levels increased.

From the results of the 2002 data alone and in conjunction with the results from earlier AFHS follow-up examinations, there was no consistent evidence to suggest that herbicide or dioxin exposure was associated with ill effects on respiratory health.

20.4 SUMMARY

The pulmonary assessment was based on questionnaire data, which was subsequently verified by a review of medical records, physical examination data, and pulmonary laboratory data. Associations with herbicide exposure (i.e., group – Model 1), initial dioxin (Model 2), categorized dioxin (Model 3), and 1987 dioxin levels (Model 4) were examined for each variable in the pulmonary assessment. The significant adjusted results are discussed in the sections below.

20.4.1 Model 1: Group Analysis

The results of the group analysis are provided in Table 20-15. A significantly greater percentage of Ranch Hand than Comparison enlisted flyers had a history of pneumonia. Significantly fewer Ranch Hand enlisted flyers than Comparison enlisted flyers were judged to have a mild obstructive abnormality.

Table 20-15. Summary of Group Analysis (Model 1) for Pulmonary Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	All	Officer	Enlisted Flyer	Enlisted Groundcrew
Medical Records				
Asthma (D)	NS	NS	ns	NS
Bronchitis (D)	NS	ns	NS	NS
Pneumonia (D)	ns	ns	p=0.049 (1.91)	ns
Physical Examination				
Thorax and Lung Abnormality (D)	p=0.039 (1.28)	NS	p=0.041 (1.68)	NS
Laboratory				
X-ray Interpretation (D)	ns	ns	NS	ns
FVC (C)[a]	ns	ns	ns	ns
FVC (D)	ns	NS	ns	ns
FEV_1 (C)[a]	ns	ns	ns	ns
FEV_1 (D)	NS	NS	NS	ns
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	ns	NS	NS
Loss of Vital Capacity (D)				
Mild vs. None	ns	ns	ns	ns
Moderate or Severe vs. None	ns	NS	ns	ns
Obstructive Abnormality (D)				

	UNADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Mild vs. None	NS	NS	ns	NS
Moderate vs. None	ns	NS	ns	ns
Severe vs. None	NS	NS	ns	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: NS or ns: Not significant (p>0.05).
    C: Continuous form of dependent variable.
    D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

	ADJUSTED			
Variable	**All**	**Officer**	**Enlisted Flyer**	**Enlisted Groundcrew**
Medical Records				
Asthma (D)	NS	NS	ns	NS
Bronchitis (D)	NS	ns	NS	NS
Pneumonia (D)	ns	ns	p=0.046 (1.94)	ns
Physical Examination				
Thorax and Lung Abnormality (D)	NS	NS	NS	NS
Laboratory				
X-ray Interpretation (D)	ns	ns	NS	ns
FVC (C)[a]	ns	ns	ns	ns
FVC (D)	ns	ns	ns	ns
FEV_1 (C)[a]	ns	ns	ns	ns
FEV_1 (D)	NS	NS	NS	ns
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	ns	NS	NS
Loss of Vital Capacity (D)				
Mild vs. None	ns	ns	ns	ns
Moderate or Severe vs. None	ns	NS	ns	ns
Obstructive Abnormality (D)				
Mild vs. None	NS	NS	p=0.046 (0.59)	NS
Moderate vs. None	ns	NS	ns	ns
Severe vs. None	NS	NS	ns	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: NS or ns: Not significant (p>0.05).
     C: Continuous form of dependent variable.
     D: Discrete form of dependent variable.

The p-value was given if $p \leq 0.05$. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

20.4.2 Model 2: Initial Dioxin Analysis

Associations between initial dioxin and the dependent variables were examined in the Model 2 analyses. The results are shown in Table 20-16. As initial dioxin increased, the ratio of the observed FEV_1 to the observed FVC increased. The percentage of Ranch Hands with a moderate obstructive abnormality decreased as initial dioxin increased. The percentage of Ranch Hands with a severe obstructive abnormality decreased as initial dioxin increased.

Table 20-16. Summary of Initial Dioxin Analysis (Model 2) for Pulmonary Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Asthma (D)	ns	ns
Bronchitis (D)	NS	NS
Pneumonia (D)	ns	ns
Physical Examination		
Thorax and Lung Abnormality (D)	NS	ns
Laboratory		
X-ray Interpretation (D)	p=0.040 (0.80)	ns
FVC (C)[a]	NS	ns
FVC (D)	ns	ns
FEV_1 (C)[a]	NS	NS
FEV_1 (D)	ns	NS
Ratio of Observed FEV_1 to Observed FVC (C)[b]	p=0.004 (-0.032)	p=0.039 (-0.023)
Loss of Vital Capacity (D)		
Mild vs. None	ns	ns
Moderate or Severe vs. None	ns	ns
Obstructive Abnormality (D)		
Mild vs. None	p=0.019 (0.82)	ns
Moderate vs. None	p=0.016 (0.67)	p=0.023 (0.64)
Severe vs. None	p=0.022 (0.50)	p=0.036 (0.44)

[a]A negative slope was considered adverse for this variable.

[b]A positive slope was considered adverse for this variable; a negative slope implies an increase in the ratio because of the data transformation used.

Note: NS or ns: Not significant (p>0.05).
       C: Continuous form of dependent variable.
       D: Discrete form of dependent variable.

       The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

       A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

20.4.3 Model 3: Categorized Dioxin Analysis

The results of the categorized dioxin analysis are presented in Table 20-17. Ranch Hands in the low dioxin category had a significantly lower mean FVC than Comparisons. No other significant differences between Ranch Hands and Comparisons were found in Model 3 analyses.

Table 20-17. Summary of Categorized Dioxin Analysis (Model 3) for Pulmonary Variables (Ranch Hands vs. Comparisons)

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Medical Records				
Asthma (D)	NS	ns	ns	ns
Bronchitis (D)	NS	NS	NS	NS
Pneumonia (D)	ns	NS	ns	ns
Physical Examination				
Thorax and Lung Abnormality (D)	NS	NS	NS	p=0.025 (1.37)
Laboratory				
X-ray Interpretation (D)	ns	NS	ns	ns
FVC (C)[a]	NS	p=0.001 (-3.86)	ns	p=0.005 (-2.58)
FVC (D)	ns	NS	ns	ns
FEV$_1$ (C)[a]	ns	p=0.002 (-4.11)	ns	p=0.033 (-2.12)
FEV$_1$ (D)	NS	p=0.039 (1.39)	ns	NS
Ratio of Observed FEV$_1$ to Observed FVC (C)[a]	ns	ns	p=0.027 (0.013)	NS
Loss of Vital Capacity (D)				
Mild vs. None	p=0.027 (0.47)	NS	ns	ns
Moderate or Severe vs. None	NS	NS	ns	ns

Variable	UNADJUSTED			
	Background Ranch Hands vs. Comparisons	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Obstructive Abnormality (D)				
Mild vs. None	NS	NS	ns	ns
Moderate vs. None	ns	NS	ns	ns
Severe vs. None	NS	NS	ns	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: NS or ns: Not significant (p>0.05).
      C: Continuous form of dependent variable.
      D: Discrete form of dependent variable.

      The p-value was given if $p \leq 0.05$. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

      A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

Variable	ADJUSTED			
	Background Ranch Hands vs. Comparisons	**Low Ranch Hands vs. Comparisons**	**High Ranch Hands vs. Comparisons**	**Low plus High Ranch Hands vs. Comparisons**
Medical Records				
Asthma (D)	NS	ns	ns	ns
Bronchitis (D)	NS	NS	NS	NS
Pneumonia (D)	ns	NS	ns	ns
Physical Examination				
Thorax and Lung Abnormality (D)	NS	NS	NS	NS
Laboratory				
X-ray Interpretation (D)	ns	ns	ns	ns
FVC (C)[a]	NS	p=0.031 (-2.52)	ns	ns
FVC (D)	ns	NS	ns	ns
FEV_1 (C)[a]	ns	ns	ns	ns
FEV_1 (D)	NS	NS	ns	NS
Ratio of Observed FEV_1 to Observed FVC (C)[a]	ns	ns	NS	NS
Loss of Vital Capacity (D)				
Mild vs. None	ns	ns	ns	ns
Moderate or Severe vs. None	NS	NS	ns	ns
Obstructive Abnormality (D)				
Mild vs. None	NS	NS	ns	NS
Moderate vs. None	ns	NS	ns	ns
Severe vs. None	NS	NS	ns	ns

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: NS or ns: Not significant (p>0.05).
       C: Continuous form of dependent variable.
       D: Discrete form of dependent variable.

       The p-value was given if p≤0.05. The difference in means was given in parentheses for a significant result from the analysis of a continuous dependent variable.

       A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

20.4.4   Model 4: 1987 Dioxin Level Analysis

The results of the analysis of associations between 1987 dioxin and the dependent variables examined for the pulmonary assessment are displayed in Table 20-18. No significant associations were found in the adjusted analysis of these variables.

Table 20-18. Summary of 1987 Dioxin Analysis (Model 4) for Pulmonary Variables (Ranch Hands Only)

Variable	Unadjusted	Adjusted
Medical Records		
Asthma (D)	ns	ns
Bronchitis (D)	NS	ns
Pneumonia (D)	ns	ns
Physical Examination		
Thorax and Lung Abnormality (D)	NS	ns
Laboratory		
X-ray Interpretation (D)	ns	ns
FVC (C)[a]	p<0.001 (-1.419)	ns
FVC (D)	NS	ns
FEV_1 (C)[a]	ns	ns
FEV_1 (D)	NS	NS
Ratio of Observed FEV_1 to Observed FVC (C)[b]	p<0.001 (-0.031)	ns
Loss of Vital Capacity (D)		
Mild vs. None	NS	NS
Moderate or Severe vs. None	ns	ns
Obstructive Abnormality (D)		
Mild vs. None	p=0.009 (0.88)	ns
Moderate vs. None	ns	ns
Severe vs. None	ns	ns

[a]A negative slope was considered adverse for this variable.

[b]A positive slope was considered adverse for this variable; a negative slope implies an increase in the ratio because of the data transformation used.

Note: NS or ns: Not significant (p>0.05).
       C: Continuous form of dependent variable.
       D: Discrete form of dependent variable.

The p-value was given if p≤0.05. The relative risk was given in parentheses for a significant result from the analysis of a discrete dependent variable. The slope was given in parentheses for a significant result from the analysis of a continuous dependent variable.

A capital "NS" denotes a nonsignificant positive association. A lowercase "ns" denotes a nonsignificant inverse association.

20.4.5 Summary of Significant Results

Table 20-19 summarizes the significant results (p≤0.05) for the adjusted analyses that were performed for the pulmonary assessment. The dependent variable and its table reference are listed, along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and is explained in footnotes.

Table 20-19. Summary of Results from Significant Adjusted Analyses in the Pulmonary Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Pneumonia (20-5)	1	RH vs. C, Enlisted Flyer	0.046	1.94 (1.01,3.72)	RH: 19.7% C: 11.4%	(a)
FVC (20-8)[a]	3	Low RH vs. C	0.031	-2.52 (-4.81,-0.23)	RH: 93.22 percent C: 95.74 percent	(b)
Ratio of Observed FEV_1 to Observed FVC (20-12)[b]	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.039	-0.023 (0.011)	Low: 0.729 Medium: 0.740 High: 0.752	(c)
Obstructive Abnormality (20-14)	1	RH vs. C, Enlisted Flyer – mild vs. none	0.046	0.59 (0.35,0.99)	RH: 34.1% C: 43.1%	(a)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin – moderate vs. none	0.023	0.64 (0.43,0.94)	Low: 11.7% Medium: 8.6% High: 2.9%	(d)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin – severe vs. none	0.036	0.44 (0.20,0.95)	Low: 4.4% Medium: 4.3% High: 0.0%	(d)

Table 20-19. Summary of Results from Significant Adjusted Analyses in the Pulmonary Assessment (Continued)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(b): Continuous variable: difference of adjusted means and 95% confidence interval were presented; adjusted means were presented for each dioxin category in contrast.

(c): Continuous variable: slope and standard error were presented and were based on natural logarithm of 1.0 - dependent variable) versus $\log_2$ (initial dioxin); adjusted means were presented for each of three initial dioxin categories.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal was presented for each of three initial dioxin categories.

[a]A smaller group mean was considered adverse for this variable.
[b]A positive slope was considered adverse for this variable; a negative slope implies an increase in the ratio because of the data transformation used.

Note: RH = Ranch Hand.
        C = Comparison.

        Model 2: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt).

        Model 3: Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
        Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
        High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

20.5 CONCLUSION

The AFHS assessed respiratory health by investigating the occurrence of asthma, bronchitis, and pneumonia, and the presence of an abnormality on physical examination of the thorax and lungs and as seen on a chest x-ray film. The pulmonary assessment also investigated lung function as measured by FVC, FEV_1, the FEV_1 to FVC ratio, and the severity of obstructive abnormality and loss of vital capacity.

Statistically significant findings indicating adverse effects on Ranch Hands were limited to pneumonia and FVC. A significantly greater percentage of Ranch Hand than Comparison enlisted flyers had a history of pneumonia. Ranch Hands in the low dioxin category had a significantly lower mean FVC than Comparisons. No other significant findings adverse to Ranch Hands were observed.

No consistent evidence suggested that herbicides or dioxin were associated with ill effects on respiratory health.

REFERENCES

1. McKinney, W.P., D.D. McIntire, T.J. Carmody, and A. Joseph. 1997. Comparing the smoking behavior of veterans and nonveterans. Public Health Reports 112:212-7 (discussion 8).

2. Institute of Medicine. 1997. Veterans and Agent Orange: Update 1996. National Academy Press: Washington, DC.

3. Institute of Medicine. 2001. Veterans and Agent Orange: Update 2000. National Academy Press: Washington, DC.

4. Tuteja, N., F.J. Gonzalez, and D.W. Nebert. 1985. Developmental and tissue-specific differential regulation of the mouse dioxin-inducible P1-450 and P3-450 genes. *Developmental Biology* 112:177-84.

5. Kurl, R.N., K.C. Chaudhary, and C.A. Villee. 1986. Characterization and control of cytosolic binding proteins for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the rat lung. *Pharmacology* 33:181-9.

6. Devereux, T.R., M.W. Anderson, and S.A. Belinsky. 1988. Factors regulating activation and DNA alkylation by 4-(N-methyl-N-nitrosamino)-1-(3-pyridyl)-1-butanone and nitrosodimethylamine in rat lung and isolated lung cells, and the relationship to carcinogenicity. *Cancer Research* 48:4215-21.

7. Domin, B.A., T.R. Devereux, J.R. Fouts, and R.M. Philpot. 1986. Pulmonary cytochrome P-450: Isozyme profiles and induction by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in clara and type II cells and microphages isolated from rabbit lung. *Federal Proceedings* 45:321.

8. Domin, B.A., T.R. Devereux, and R.M. Philpot. 1986. The cytochrome P-450 monooxygenase system of rabbit lung enzyme components, activities, and induction in the nonciliated bronchiolar epithelial (Clara) cell, alveolar type II cell, and alveolar macrophage. *Molecular Pharmacology* 30:296-303.

9. Domin, B.A., and R.M. Philpot. 1986. The effect of substrate on the expression of activity catalyzed by cytochrome P-450: Metabolism mediated by rabbit isozyme 6 in pulmonary microsomal and reconstituted monooxygenase systems. *Archives of Biochemistry and Biophysics* 246:128-42.

10. Vanderslice, R.R., B.A. Domin, G.T. Carver, and R.M. Philpot. 1987. Species-dependent expression and induction of homologues of rabbit cytochrome P-450 isozyme 5 in liver and lung. *Molecular Pharmacology* 31:320-5.

11. Mathews, J.M., and J.R. Bend. 1986. N-alkylaminobenzotriazoles as isozyme-selective suicide inhibitors of rabbit pulmonary microsomal cytochrome P-450. *Molecular Pharmacology* 30:25-32.

12. Overby, L.H., S. Nishio, A. Weir, G.T. Carver, C.G. Plopper, and R.M. Philpot. 1992. Distribution of cytochrome P450 1A1 and NADPH-cytochrome P450 reductase in lungs of rabbits treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin: Ultrastructural immunolocalization and in situ hybridization. *Molecular Pharmacology* 41:1039-46.

13. Iba, M.M., and J. Fung. 2001. Pulmonary Cyp1A1 and CYP1A2 levels and activities in adult male and female offspring of rats exposed during gestation and lactation to 2,3,7, 8-tetrachlorodibenzo-p-dioxin. *Biochemical Pharmacology* 62:617-26.

14. Wei, C., R.J. Caccavale, J.J. Kehoe, P.E. Thomas, and M.M. Iba. 2001. CYP1A2 is expressed along with CYP1A1 in the human lung. *Cancer Letters* 171:113-20.

15. Beebe, L.E., S.S. Park, and L.M. Anderson. 1990. Induction responses in mouse liver and lung following a single intraperitoneal dose of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). *Federation of American Societies for Experimental Biology Journal* 4:A345.

16. Nessel, C.S., M.A. Amoruso, T.H. Umbreit, and M.A. Gallo. 1990. Hepatic aryl hydrocarbon hydroxylase and cytochrome P450 induction following the transpulmonary absorption of TCDD from intratracheally instilled particles. *Fundamental and Applied Toxicology* 15:500-9.

17. Nessel, C.S., M.A. Amoruso, T.H. Umbreit, R.J. Meeker, and M.A. Gallo. 1989. Induction of cytochrome P-450 as a marker of the transpulmonary absorption of TCDD. *Toxicologist* 9:120.

18. Institute of Medicine. 2002. Herbicide/dioxin exposure and acute myelogenous leukemia in the children of Vietnam veterans. National Academy Press: Washington, DC.

19. Zack, J.A., and R.R. Suskind. 1980. The mortality experience of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident. *Journal of Occupational Medicine* 22:11-4.

20. Sweeney, M.H., and P. Mocarelli. 2000. Human health effects after exposure to 2,3,7,8-TCDD. *Food Additives and Contaminants* 17:303-16.

21. Pesatori, A.C., C. Zocchetti, S. Guercilena, D. Consonni, D. Turrini, and P.A. Bertazzi. 1998. Dioxin exposure and non-malignant health effects: A mortality study. *Occupational and Environmental Medicine* 55:126-31.

22. Bertazzi, P.A., I. Bernucci, G. Brambilla, D. Consonni, and A.C. Pesatori. 1998. The Seveso studies on early and long-term effects of dioxin exposure: A review. *Environmental Health Perspectives* 106(Suppl 2):625-33.

23. Bertazzi, P.A., D. Consonni, S. Bachetti, M. Rubagotti, A. Baccarelli, C. Zocchetti, and A.C. Pesatori. 2001. Health effects of dioxin exposure: A 20-year mortality study. *American Journal of Epidemiology* 153:1031-44.

24. Suskind, R.R., and V.S. Hertzberg. 1984. Human health effects of 2,4,5-T and its toxic contaminants. *The Journal of the American Medical Association* 251:2372-80.

25. Zober, A., M.G. Ott, and P. Messerer. 1994. Morbidity follow up study of BASF employees exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after a 1953 chemical reactor incident. *Occupational and Environmental Medicine* 51:479-86.

26. Calvert, G.M., M.H. Sweeney, J.A. Morris, M.A. Fingerhut, R.W. Hornung, and W.E. Halperin. 1991. Evaluation of chronic bronchitis, chronic obstructive pulmonary disease, and ventilatory function among workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *American Review of Respiratory Disease* 144:1302-6.

27. Sweeney, M.H., G.M. Calvert, G.A. Egeland, M.A. Fingerhut, W.E. Halperin, and L.A. Piacitelli. 1997. Review and update of the results of the NIOSH medical study of workers exposed to chemicals contaminated with 2,3,7,8-tetrachlorodibenzodioxin. *Teratogenesis, Carcinogenesis, and Mutagenesis* 17:241-7.

28. Collins, J.J., M.E. Strauss, G.J. Levinskas, and P.R. Conner. 1993. The mortality experience of workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin in a trichlorophenol process accident. *Epidemiology* 4:7-13.

29. Ramlow, J.M., N.W. Spadacene, S.R. Hoag, B.A. Stafford, J.B. Cartmill, and P.J. Lerner. 1996. Mortality in a cohort of pentachlorophenol manufacturing workers, 1940-1989. *American Journal of Industrial Medicine* 30:180-94.

30. Becher, H., D. Flesch-Janys, T. Kauppinen, M. Kogevinas, K. Steindorf, A. Manz, and J. Wahrendorf. 1996. Cancer mortality in German male workers exposed to phenoxy herbicides and dioxins. *Cancer Causes and Control* 7:312-21.

31. Ott, M.G., and A. Zober. 1996. Cause specific mortality and cancer incidence among employees exposed to 2,3,7,8-TCDD after a 1953 reactor accident. *Occupational and Environmental Medicine* 53:606-12.

32. Kogevinas, M., H. Becher, T. Benn, P.A. Bertazzi, P. Boffetta, H.B. Bueno-de-Mesquita, D. Coggon, D. Colin, D. Flesch-Janys, M. Fingerhut, L. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, N. Pearce, and R. Saracci. 1997. Cancer mortality in workers exposed to phenoxy herbicides, chlorophenols, and dioxins. An expanded and updated international cohort study. *American Journal of Epidemiology* 145:1061-75.

33. Vena, J., P. Boffetta, H. Becher, T. Benn, H.B. Bueno-de-Mesquita, D. Coggon, D. Colin, D. Flesch-Janys, L. Green, T. Kauppinen, M. Littorin, E. Lynge, J.D. Mathews, M. Neuberger, N. Pearce, A.C. Pesatori,, R. Saracci, K. Steenland, and M. Kogevinas. 1998. Exposure to dioxin and nonneoplastic mortality in the expanded IARC international cohort study of phenoxy herbicide and chlorophenol production workers and sprayers. *Environmental Health Perspectives* 106(Suppl 2):645-53.

34. Steenland, K., L. Piacitelli, J. Deddens, M. Fingerhut, and L.I. Chang. 1999. Cancer, heart disease, and diabetes in workers exposed to 2,3,7,8- tetrachlorodibenzo-p-dioxin. *Journal of the National Cancer Institute* 91:779-86.

35. U.S. Centers for Disease Control. 1988. Health status of Vietnam veterans. II. Physical health. *The Journal of the American Medical Association* 259:2708-14.

36. Pollei, S., F.A. Mettler, Jr., C.A. Kelsey, M.R. Walters, and R.E. White. 1986. Follow-up chest radiographs in Vietnam veterans: Are they useful? *Radiology* 161:101-2.

37. Stellman, S.D., J.M. Stellman, and J.F. Sommer, Jr. 1988. Health and reproductive outcomes among American Legionnaires in relation to combat and herbicide exposure in Vietnam. *Environmental Research* 47:150-74.

38. O'Toole, B.I., R.P. Marshall, D.A. Grayson, R.J. Schureck, M. Dobson, M. Ffrench, B. Pulvertaft, L. Meldrum, J. Bolton, and J. Vennard. 1996. The Australian Vietnam veterans health study: II. Self-reported health of veterans compared with the Australian population. *International Journal of Epidemiology* 25:319-30.

39. Michalek, J.E., N.S. Ketchum, and F.Z. Akhtar. 1998. Postservice mortality of US Air Force veterans occupationally exposed to herbicides in Vietnam: 15-year follow-up. *American Journal of Epidemiology* 148:786-92.

40. Crane, P.J., D.L. Barnard, K.D. Horsley, and M.A. Adena. 1997. Mortality of National Service Vietnam Veterans: A report of the 1996 retrospective cohort study of Australian Vietnam veterans. Department of Veterans Affairs: Canberra.

41. Dalager, N.A., and H.K. Kang. 1997. Mortality among Army Chemical Corps Vietnam veterans. *American Journal of Industrial Medicine* 31:719-26.

42. Thomas, W.F., W.D. Grubbs, T.G. Karrison, M.B. Lustik, R.H. Roegner, D.E. Williams, W.H. Wolfe, J.E. Michalek, J.C. Miner, and R.W. Ogershok. 1990. An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: 1987 followup examination results, May 1987 to January 1990. NTIS: AD A 222 573. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

43. Grubbs, W.D., W.H. Wolfe, J.E. Michalek, D.E. Williams, M.B. Lustik, A.S. Brockman, S.C. Henderson, F.R. Burnett, R.G. Land, D.J. Osborne, V.K. Rocconi, M.E. Schreiber, J.C. Miner, G.L. Henriksen, and J.A. Swaby. 1995. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1992 followup examination results. NTIS: AD A 304 306, 304 308-316. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

44. Michalek, J.E., B.R. Burnham, H.E. Marden, Jr., J.N. Robinson, V.V. Elequin, J.C. Miner, R.W. Ogershok, W.K. Sneddon, W.D. Grubbs, B.C. Cooper, R.G. Land, V.K. Rocconi, M.E. Yeager, D.E. Williams, and M.E.B. Owens. 2000. The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides: Final report. 1997 follow-up examination results. USAF School of Aerospace Medicine, Brooks Air Force Base, TX.

45. Renzetti, A.D., E.R. Bleecker, G.R. Epler, G.R. Jones, R.E. Kanner, and L.H. Repsher. 1986. American Thoracic Society (ATS) statement-evaluation of impairment/disability secondary to respiratory disorders. *The American Review of Respiratory Disease* 133:1205-9.

46. Garrow, J.S., and J. Webster. 1985. Quetelet's index (W/H^2) as a measure of fatness. *International Journal of Obesity* 9:147-53.

47. Patterson, D.G., Jr., L. Hampton, C.R. Lapeza, Jr., W.T. Belser, V. Green, L.R. Alexander, and L.L. Needham. 1987. High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid weight basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Annals of Chemistry* 59:2000-5.

48. Michalek, J.E., and R.C. Tripathi. 1999. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 15-year follow-up. *Journal of Toxicology and Environmental Health* 57:369-78.

49. American Thoracic Society. 1991. Lung function testing: Selection of reference values and interpretative strategies. *American Review of Respiratory Disease* 144:1202-18.

Table of Contents

21 CONCLUSIONS

21.1 INTRODUCTION

This section summarizes the conclusions drawn from the statistical analyses of data from the 2002 follow-up examination of the Air Force Health Study (AFHS). This analysis was restricted to participants who attended the 2002 follow-up examination and was an extension of the baseline, 1985, 1987, 1992, and 1997 follow-up examinations. Health endpoints measured at the 2002 examination were analyzed for associations with herbicide exposure and body burden of serum dioxin. In addition, the cumulative disease prevalence from the time of duty in Southeast Asia (SEA) to 2002 was analyzed for associations with herbicide exposure and serum dioxin body burden. A full explanation of the study design and methodology, terminology, and interpretive considerations is provided in Chapters 1 through 8 of this report.

In January 1962, President John F. Kennedy approved a program of aerial herbicide spraying for the purpose of defoliation and crop destruction in support of military operations in the Republic of Vietnam (RVN). This program, code-named Operation Ranch Hand, dispersed herbicides in South Vietnam from 1962 to 1971. Members of the Ranch Hand cohort were responsible for the spraying of the herbicides in the RVN. Comparison veterans flew and serviced C-130 transport planes in SEA during the same time period that the Ranch Hand unit was active but did not engage in spraying operations.

Throughout this report, dioxin levels were used as measures of both exposure to dioxin itself and exposure to dioxin-contaminated herbicides, including Agent Orange. Direct contrasts of Ranch Hand and Comparison veterans address the hypothesis of health effects attributable to any herbicide exposure experienced by Ranch Hand veterans during Operation Ranch Hand. Models involving dioxin levels address the hypothesis that health effects change with the amount of exposure. Serum dioxin levels were used as a measure of exposure to dioxin-contaminated herbicides because it was expected that as exposure to such herbicides increased, serum dioxin levels should increase. The serum dioxin levels, therefore, served as a direct biomarker of exposure to dioxin-contaminated herbicides. Currently, no other direct measure or estimate of herbicide exposure is available to address hypothetical dose-response relations with health. Some indirect measures, such as self-report of skin contact among enlisted groundcrew, or simply being a Ranch Hand enlisted groundcrew member, are valuable alternatives because dioxin measures suggest that enlisted groundcrew experienced the heaviest exposures. Reported skin exposure was not addressed in this report, but enlisted groundcrew status was used in contrasts of Ranch Hand and Comparison veterans. The use of dioxin as a surrogate measure of exposure to dioxin-contaminated herbicides is consistent with the goal of the study, which is to determine whether health effects exist and can be attributed to occupational exposure to Agent Orange.

21.2 STUDY PERFORMANCE ASPECTS

A total of 1,951 veterans participated in the 2002 follow-up examination. Participation was voluntary and consent forms were signed at the examination site. Of the 1,043 eligible Ranch Hands, 777 (74.5%) participated in the 2002 follow-up examination. A total of 737 of the 1,093 eligible Original Comparisons (67.4%) and 437 (46.0%) of the 951 eligible Replacement Comparisons participated in the 2002 follow-up examination. There was no evidence of compliance bias in this study.

Nearly the same percentages of Ranch Hands, Original Comparisons, and Replacement Comparisons refused due to health reasons. The number of Ranch Hands who refused for health reasons, logistical

reasons, passive refusals, and hostile refusals were approximately equal. The Comparisons, however, were classified as passive refusals or refused for logistical reasons more often than being classified as a hostile refusal or providing health concerns as the reason for refusal.

Reported health status (excellent, good, fair, or poor) differed with age, military rank, and compliance status among those reporting their health status at the time of scheduling for the 2002 follow-up examination. After adjusting for age, military rank, race, and compliance status, Ranch Hands were found to be more likely to report fair or poor health than Comparisons. This pattern of Ranch Hands reporting poorer health had been observed since the baseline examination.

Work loss due to illness or injury in the 6 months prior to the 2002 follow-up physical examination and participant-reported medication were used as alternative indicators of health. No difference was seen in reported work loss or in medication use between Ranch Hands and Comparisons. A further analysis of self-perception of health, as reported by fully compliant participants at the 2002 follow-up examination, is given in Chapter 9, General Health Assessment.

21.3 STATISTICAL MODELS

The analysis of the 2002 follow-up examination results used four statistical models to evaluate the relation between the health status of study participants and their herbicide exposure or serum dioxin levels. The first model specified contrasts between Ranch Hands and Comparisons using these groups as a proxy for herbicide exposure and did not incorporate serum dioxin measurements. The remaining three models all incorporated serum dioxin measurements in either 1987 dioxin levels or an estimate of an initial dioxin level based on a first-order extrapolation to the end of the qualifying tour of duty in SEA. The four models are summarized as follows:

- Model 1: Ranch Hands versus Comparisons, for all military occupations (officer, enlisted flyer, enlisted groundcrew) combined and for each military occupation separately

- Model 2: Estimated initial serum dioxin levels at end of qualifying tour using Ranch Hand participants with greater than 10 parts per trillion (ppt) of first-measured lipid-adjusted dioxin

- Model 3: Ranch Hands categorized according to 1987 and initial serum dioxin levels (background, low, and high) versus Comparisons

- Model 4: First-measured lipid-adjusted serum dioxin using Ranch Hands only. The measurement was extrapolated to 1987 only if the measurement was over 10 ppt.

Statistical analyses often were applied to clinical endpoints in continuous form (i.e., original measurements), as well as in discrete form (i.e., measurements grouped into categories based on abnormal levels). Analyses also were performed to account for the effects that demographic and personal characteristics (covariates) may have had on the clinical measurements. Such analyses were termed "adjusted analyses." The relation between health and the measures of herbicide exposure or dioxin level in the four models described above are summarized in the next section. The relation between covariates and measures of herbicide exposure or dioxin level are described in Chapter 8.

21.4 CLINICAL RESULTS

This section provides the conclusions from the analyses of the 12 clinical areas—general health, neoplasia, neurology, psychology, gastrointestinal, dermatology, cardiovascular, hematology, renal, endocrine, immunology, and pulmonary. Tables G-1 through G-24 of Appendix G present the results of

the exposure analyses for each of the four models for more than 300 health endpoints analyzed in the 12 clinical chapters. Appendix H contains a summary of significant results ($p \leq 0.05$) for the adjusted analyses that were performed for the group and dioxin analyses (Models 1-4) in the 12 clinical areas. All findings described in the subsequent sections were significant and adjusted for covariates.

21.4.1   General Health Assessment

Four variables were included in the general health assessment: self-perception of health, appearance of illness or distress during the examination, relative age, and body mass index. For the evaluation of self-perception of health, each participant was asked to rate his health (excellent, good, fair, poor) compared to other people his age. In addition, a board-certified internist examined the participants for the appearance of acute illness or distress (yes or no). The internist assessed whether each subject appeared younger than, older than, or the same as his stated age to determine relative age. Body mass index was computed based on height and weight recorded at the physical examination.

Self-perception of health, appearance of illness, and relative age appearance were not found to be associated with herbicide exposure (Ranch Hand versus Comparison) or dioxin level. Body mass index was positively associated with 1987 dioxin, possibly reflecting the pharmacokinetics of dioxin elimination.

21.4.2   Neoplasia Assessment

During the 2002 health interview, each study participant was asked a series of questions on the occurrence of cancer since the date of his last health interview. The self-reported conditions were verified by a medical records review and combined with cancer information collected at previous AFHS examinations. For chest x-ray findings that were reported as needing follow-up at the 2002 physical examination, the AFHS made every effort to contact and encourage participants to see their physicians. The participants were recontacted to determine a final diagnosis. Some possible neoplastic conditions were discovered by the physicians at the physical examination. Contingent upon participant authorization, suspicious skin lesions were biopsied and the pathology determined; no other invasive procedures were used to detect systemic neoplasms.

Skin neoplasms were analyzed by behavior type and cell type. Systemic neoplasms were analyzed by behavior and anatomical site. All skin and systemic neoplasms and all malignant skin and systemic neoplasms also were analyzed. Analyses were conducted on prostate-specific antigen, which was used to detect prostate enlargement and prostate cancer.

Contrasts of Ranch Hands with Comparisons by military occupation showed significant results only for officers. Ranch Hand officers had an increased risk of basal cell carcinoma and, consequently, nonmelanoma skin cancers. Ranch Hand officers also had an increased risk of malignant systemic neoplasms. The analysis of malignant systemic neoplasms of the colon and rectum and of the urinary system showed a greater risk for Ranch Hand officers.

The prevalence of a malignant systemic neoplasm of the urinary system increased as initial dioxin in Ranch Hands increased.

When comparing categorized levels of dioxin, significant results were primarily found when comparing Ranch Hands in the low dioxin category with Comparisons. Ranch Hands in the low dioxin category had an increased risk of a basal cell carcinoma and, consequently, this pattern was also seen in nonmelanoma skin cancers, malignant skin cancers, and all skin neoplasms (benign, malignant, and uncertain behavior).

The risk of a skin neoplasm of uncertain behavior or unspecified nature was also increased for Ranch Hands in the low dioxin category.

The prevalence of a malignant systemic neoplasm, combined across sites, also was increased for Ranch Hands in the low dioxin category relative to Comparisons. Results of the site-specific analyses included increased risks to Ranch Hands in the low dioxin category for malignant systemic neoplasms of the bronchus or lung, colon or rectum, and prostate. These findings led to an increased risk for Ranch Hands in the low dioxin category for all neoplasms and all malignant neoplasms (combining skin and systemic). Ranch Hands in the background category had an increased risk of a malignant systemic neoplasm of the urinary system. Ranch Hands in the low and high dioxin categories combined had an increased prevalence of a skin neoplasm of any type.

The associations between dioxin levels and the likelihood of developing cancer were seen primarily for Ranch Hand officers and Ranch Hands in the low dioxin category, which were the lower-exposed subgroups, on average. Some of these associations also may have been due to chance or to a lack of adjustment for a factor not considered in these analyses.

21.4.3 Neurology Assessment

The neurology assessment included the evaluation of cranial nerve function, peripheral nerve status, and central nervous system (CNS) coordination processes based on a physical examination. The cranial nerve function incorporated smell, visual fields, light reaction, ocular movement, facial sensation, corneal reflex, jaw clench, smile, palpebral fissure, balance, gag reflex, speech, tongue position relative to midline, palate and uvula movement, and shoulder shrug. Peripheral nerve status was assessed by light pinprick, light touch (with cotton sticks), visual inspection of muscle mass (and palpation, if indicated), three deep tendon reflexes (patellar, Achilles, and biceps), and the Babinski reflex. In addition, indices of bilateral symmetric distal sensory or sensorimotor polyneuropathy were analyzed based on testing of ankle and toe flexor strength, equilibrium (Romberg sign), Achilles reflex, light touch, pinprick, vibration at the ankle, and joint position of the left and right great toes. The evaluation of CNS coordination processes was based on tremor, coordination, Romberg sign, and gait.

Ranch Hands were more likely to have abnormal visual fields and an abnormal cranial nerve index than Comparisons. More Ranch Hand officers had hereditary or degenerative diseases and sluggish or absent Achilles reflexes than Comparison officers.

Positive associations were seen between balance and coordination and extrapolated initial dioxin levels.

Analyses based on dioxin category showed an increased risk of abnormal visual fields in the background dioxin category and an increased risk of abnormal facial sensation for Ranch Hands in the low dioxin category. Ranch Hands in both the background and low dioxin categories showed an increased risk of abnormalities for the cranial nerve index, a composite index of the individual 15 cranial nerve endpoints studied in this assessment. More Ranch Hands in the high dioxin category had an abnormal reaction to pinprick and absent patellar reflexes than Comparisons.

Analyses of 1987 dioxin levels showed a positive association with the absence of the patellar reflex.

Based on the results of the analysis of pinprick, balance, and the patellar reflex in this follow-up examination, there was some limited support of an association between dioxin levels and neurological disease related to the peripheral nerves. In conclusion, there was no clinical evidence to support a relation between dioxin and cranial nerve function or other CNS processes.

21.4.4 Psychology Assessment

The Symptom Checklist-90-Revised (SCL-90-R) and the Wechsler Memory Scale-Revised (WMS-R) were used in the psychology assessment. The SCL-90-R was used to measure symptomatic psychological distress in terms of anxiety, depression, hostility, interpersonal sensitivity, obsessive-compulsive behavior, paranoid ideation, phobic anxiety, psychoticism, and somatization. The SCL-90-R was also used to measure three global distress indices: global severity index, positive symptom total, and positive symptom distress index. The WMS-R was an instrument used for appraising major dimensions of memory functions in adolescents and adults, including memory for verbal and figural stimuli, meaningful and abstract material, and delayed as well as immediate recall. The psychological disorders of psychoses, alcohol and drug dependence, anxiety, and other neuroses, which were verified through a review of medical records, also were studied.

Ranch Hands had a smaller percentage of abnormally high scores on the SCL-90-R interpersonal sensitivity, paranoid ideation, and positive symptom total scales. Ranch Hand enlisted groundcrew had an increased mean score on the delayed recall portion of the WMS-R Logical Memory test. The percentage of abnormally high scores on the SCL-90-R phobic anxiety scale score decreased with increased 1987 dioxin levels. None of the memory functioning and psychopathology scales was adversely associated with exposure to herbicides or dioxin.

21.4.5 Gastrointestinal Assessment

The gastrointestinal assessment consisted of the analysis of (1) 7 categories of liver disorders, (2) hepatomegaly (enlarged liver), as determined at the 2002 physical examination, and (3) 28 laboratory measurements. Laboratory tests are generally considered the most reliable method for identifying acute liver disease because digestive symptoms are frequently nonspecific and intermittent and liver disorders are commonly asymptomatic. Furthermore, the detection of liver enlargement on the sole basis of a physical examination may be confounded by factors such as obesity or obstructive airway disease.

Positive stool hemoccult results were increased and mean C4 complement was decreased among Ranch Hand officers. Among enlisted groundcrew, Ranch Hands had greater percentages of abnormal alkaline phosphatase and triglyceride values than Comparisons. Ranch Hand enlisted groundcrew had a higher mean haptoglobin level.

As initial dioxin increased, C4 complement levels decreased and the percentage of Ranch Hands with abnormally low C4 complement values increased.

Ranch Hands in the low dioxin category, high dioxin category, and low and high dioxin categories combined had increased percentages of abnormally high triglyceride values. Ranch Hands in the low dioxin category and low and high dioxin categories combined had an increased prevalence of abnormally high α-1-antitrypsin values than did Comparisons. In the background dioxin category, Ranch Hands had a higher mean prothrombin time than Comparisons. In the low and high dioxin categories combined, Ranch Hands had a higher mean haptoglobin level than Comparisons.

The percentage of Ranch Hands with abnormal triglyceride values increased as 1987 dioxin increased.

There was no clear relation between herbicide exposure or dioxin levels and any of the abnormalities, although based on the analysis of triglycerides, a subtle relation between dioxin and lipid metabolism cannot be excluded.

21.4.6   Dermatology Assessment

The dermatology assessment included the occurrence of self-reported acne and physical examination. Data collected included the lifetime occurrence of acne, the occurrence of acne in relation to time of duty, and the location of acne (e.g., temples, eyes, ears). Acneiform lesions, acneiform scars, comedones, inclusion cysts, depigmentation, and hyperpigmentation were analyzed, as determined by a dermatologic examination.

The lifetime occurrence of acne and the occurrence of acne after service in SEA were greater for Ranch Hand enlisted groundcrew, the subgroup with the highest median dioxin level. Increases in self-reported acne in all Ranch Hand dioxin categories relative to Comparisons also were observed. Further study of reported lifetime acne showed that acne after service in SEA (post-SEA acne) was greater in all Ranch Hand dioxin categories relative to Comparisons only for participants who did not have acne prior to service in SEA (pre-SEA acne). As dioxin levels increased, the duration of acne increased for participants who reported acne only after service in SEA.

There were no findings of chloracne in the Ranch Hand and Comparison groups. The reasons for the higher occurrence of acne in Ranch Hand enlisted groundcrew are unknown. Reported acne was increased in Ranch Hand enlisted groundcrew, in parallel with an increase found at the 1992 physical examination. The interpretation of the increased reporting of acne among enlisted groundcrew is uncertain. Physical examination for acneiform lesions, acneiform scars, comedones, inclusion cysts, depigmentation, and hyperpigmentation, which may be suggestive of chloracne, revealed no patterns supporting a relation with herbicide exposure or dioxin.

21.4.7   Cardiovascular Assessment

In the cardiovascular assessment, data regarding cardiac function and heart disease history were studied. Variables evaluated included the lifetime history of essential hypertension, heart disease, myocardial infarction, and stroke or transient ischemic attack. The physical examination included indices of central cardiac function and peripheral vascular function. Assessment of central cardiac function was made by measuring systolic and diastolic blood pressures, heart sounds, and a resting electrocardiograph. Peripheral vascular function was assessed by presence or absence of carotid bruits, various pulse-point readings, a resting blood pressure index, measures of intermittent claudication and vascular insufficiency, and funduscopic examination of small vessels. Major risk factors for cardiovascular disease included male gender, family history, high blood cholesterol, high blood pressure, diabetes mellitus, cigarette smoking, and physical inactivity.

The presence of heart disease was found to be higher among Ranch Hands than Comparisons in enlisted flyers. Ranch Hands were found to have a lower presence of abnormal pulses, both in all participants and in the officer stratum.

An increased percentage of Ranch Hands in the high dioxin category were found to have abnormally high diastolic blood pressure. Ranch Hands in both the low dioxin category and the low and high dioxin categories combined were found to have a lower mean systolic blood pressure. Similarly, a smaller percentage of Ranch Hands in both the low dioxin category and the low and high dioxin categories combined had an abnormally high systolic blood pressure.

A lower percentage of Ranch Hands in both the background dioxin category and the low dioxin category had abnormal posterior tibial pulses. In addition, abnormal peripheral pulses were found among a lower percentage of Ranch Hands in the low dioxin category. As the 1987 dioxin level increased, the percentage of participants with abnormally high systolic blood pressure decreased.

The prevalence of cardiovascular disease was not increased in the Ranch Hand cohort. In only one analysis, that of diastolic blood pressure noted above, was there any evidence of an increased risk with increased body burden of dioxin.

21.4.8 Hematology Assessment

The hematology assessment included data from the laboratory examination. Fourteen hematologic variables were examined, including red blood cell (RBC) count, white blood cell (WBC) count, hemoglobin, hematocrit, and platelet count. The following absolute WBC counts were examined: segmented neutrophils, neutrophilic bands, lymphocytes, monocytes, eosinophils, and basophils. Fibrinogen, erythrocyte sedimentation rate (ESR), and RBC morphology were also analyzed.

The mean platelet count was increased among Ranch Hand enlisted flyers. Ranch Hand enlisted groundcrew experienced an increased risk of abnormal RBC morphology.

Ranch Hands in the high dioxin category and in the low and high dioxin categories combined had a higher percentage of abnormal RBC morphology results. In addition, Ranch Hands in the low and high dioxin combined category had an increased mean ESR. Ranch Hands in the low dioxin category had a decreased risk of abnormally low hematocrit levels.

For both the continuous and discrete forms of WBC, an inverse relation between WBC counts and 1987 dioxin levels was observed.

These data did not suggest an association between dioxin and any hematologic condition.

21.4.9 Renal Assessment

The 2002 follow-up examination included several laboratory measures of renal function and a questionnaire to ascertain historic renal disease among participants. Urinary protein and urine specific gravity were determined by dipstick methods, and hematuria and leukocyturia were measured by high-powered microscopic examination. Serum creatinine, blood urea nitrogen, urinary microalbumin, and urinary creatinine were assayed based on specimens collected from all participants. A creatinine clearance estimate was estimated using serum creatinine, age, and weight. The questionnaire provided data that identified participants with a history of kidney disease, defined as kidney trouble, kidney stones, or kidney infections, which was confirmed by a review of medical records. High values were considered adverse for all of the laboratory measurements except creatinine clearance.

Ranch Hands had a lower mean serum creatinine level, as well as a lower mean urinary microalbumin to urinary creatinine ratio. The mean urinary microalbumin to urinary creatinine ratio was higher for Comparisons than for Ranch Hands in the low dioxin category. Lower mean creatinine clearance values were observed more often among Comparisons than among Ranch Hands in the low dioxin category. An increase in mean creatinine clearance values was observed as 1987 dioxin levels increased.

The results from the renal assessment indicated no association between any marker of kidney disease and dioxin. In particular, there was no evidence that exposure to dioxin was associated with renal dysfunction, kidney stones, reduction in glomerular filtration rate, incidence of proteinuria or albuminuria, or cells in the urine.

21.4.10 Endocrinology Assessment

Questionnaire, physical examination, and laboratory data collected at the AFHS 2002 follow-up examination were used in the endocrinology assessment. Information from the questionnaire, which was

subsequently verified, included data on thyroid function and disease and diabetes and diabetic control. The physical examination of endocrine function included manual palpation of the thyroid gland and testes. Results from laboratory assays included data on 17 laboratory variables related to diabetes, glucose, insulin, gonadotropins, and thyroid hormones.

Ranch Hands had a higher mean thyroid-stimulating hormone level than Comparisons, primarily due to an increased mean among Ranch Hand officers. Ranch Hand officers also exhibited an increased mean luteinizing hormone level, an increased risk of abnormal 2-hour postprandial urinary glucose, and abnormal free testosterone.

Mean fasting insulin and the risk of diabetes requiring insulin control increased with initial dioxin. C-peptide and time to diabetes onset decreased as initial dioxin increased.

The risk of diabetes requiring insulin control was increased in the Ranch Hand high dioxin category.

An increase in the risk of diabetes requiring oral hypoglycemic or insulin control was observed as 1987 dioxin levels increased. Time to diabetes onset decreased as 1987 dioxin levels increased. The risk of an abnormally high hemoglobin A1c increased with 1987 dioxin levels.

Some findings appeared inconsistent with the results presented above, such as a decrease in the risk of 2-hour postprandial urinary glucose abnormalities with 1987 dioxin levels.

These findings appeared consistent with the previously noted association between Type 2 diabetes and dioxin in Ranch Hand veterans. Increased risks of diabetes requiring insulin control were found with initial dioxin, in the high dioxin category, and with 1987 dioxin levels. In contrast, associations between dioxin level and thyroid or gonadal hormone abnormalities were unlikely to be clinically important.

21.4.11 Immunology Assessment

The assessment of the immune system included the results of cell surface marker studies, absolute lymphocytes, quantitative immunoglobulins, and a lupus panel. Quantification of cell surface marker (phenotypic) studies was carried out with the use of reagent mouse monoclonal antibodies. Absolute lymphocytes, which indicate the density of lymphocytes in the blood, and immunoglobulins, which measure the ability of a specific B-cell subgroup to secrete a specific antibody class of molecules, were studied. Six measures from a lupus panel, which was considered a screening assay for a wide spectrum of autoimmune disorders, such as rheumatoid arthritis or systemic lupus erythematosus, also were analyzed.

Analyses revealed a positive correlation between initial dioxin level and CD20+ cell counts and a lower mean IgM level for Ranch Hand enlisted flyers.

In the lupus panel, a positive association was found between initial dioxin level and the presence of the antinuclear antibody (ANA), but the association did not appear to support a dose-response relation. Analyses of the rheumatoid factor and the anti-smooth muscle antibody revealed several differences, but the prevalence of abnormalities decreased as dioxin increased.

There was an increasing prevalence of a positive ANA in Ranch Hands with increasing initial dioxin levels. When looking at the individual autoantibodies, however, there were no consistent findings to support the presence of the ANA. Overall, there was no consistent or interpretable association between any measure of immune function and herbicide or dioxin exposure.

21.4.12 Pulmonary Assessment

The AFHS assessed respiratory health by investigating the occurrence of asthma, bronchitis, and pneumonia, and the presence of an abnormality on physical examination of the thorax and lungs and as seen on a chest x-ray film. The pulmonary assessment also evaluated lung function as measured by forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), the FEV_1 to FVC ratio, and the severity of obstructive abnormality and loss of vital capacity.

An increased percentage of Ranch Hand enlisted flyers had a history of pneumonia. Ranch Hands in the low dioxin category had a decreased mean FVC. No other significant findings adverse to Ranch Hands were observed.

No consistent evidence suggested that herbicides or dioxin were associated with ill effects on respiratory health.

21.5   STRENGTHS AND LIMITATIONS OF THIS REPORT

This study was limited by the sample size (preventing the study of rare diseases), imperfect exposure metrics, and the possible existence of other confounding factors that have not been measured. Study strengths included complete record verification of most health conditions, rigorous quality control, good participant compliance, complete population ascertainment, many years of follow-up, and adjustment for many known confounding factors.

Although many covariates were considered in this report, there are others that may be unknown and some that were measured but not used in this report. Some of the analyses in this report, therefore, may be biased due to lack of adjustment for an important confounding covariate. Recent studies of cancer in Ranch Hand veterans found that the calendar period of service in the Ranch Hand unit is an important covariate, for example, but this fact was discovered after the analytical plan for this report was already in place.

The study benefited from a two-tiered management structure based on separate but parallel program management and technical teams, an independently appointed and administered Advisory Committee, periodic review by the Institute of Medicine, and collaboration through interagency agreements between the Air Force and the Centers for Disease Control and Prevention, making the dioxin measurements possible. The management structure, oversight, carefully managed funding and contracting, and outstanding contractors all contributed to uniformly rigorous quality assurance, attention to detail, and timely task completion.

21.6   SUMMARY

Consistent with previous reports, current data indicate a significant and potentially meaningful adverse relation between serum dioxin levels and diabetes. A significant dose-response-related association was found with 1987 dioxin levels in Ranch Hands. The finding was supported by a dioxin-related increase in disease severity, a decrease in the time from exposure to first diagnosis, and an increase in fasting glucose and hemoglobin A1c in Ranch Hands. Similar patterns were observed in 1987, 1992, and 1997.

Based on the analysis of triglycerides, a subtle effect of dioxin on lipid metabolism cannot be excluded.

21.7   CONCLUSION

Diabetes represents the most important dioxin-related health problem seen in the AFHS.

APPENDIX A

APPENDIX A. POLICIES AND PROCEDURES FOR BLOOD COLLECTION AND PROCESSING FOR DIOXIN ASSAY

This appendix contains the following Scripps Clinic Policies and Procedures documents:

1. Specimen Processing
2. Shipping Specimens to Brooks City-Base.

POLICIES AND PROCEDURES

Scripps Clinic
Department of Pathology (211C)
10666 N. Torrey Pines Rd.
La Jolla, CA 92037

LABORATORY SECTION: **SPECIMEN PROCESSING**	
TITLE: **AIR FORCE HEALTH STUDY - SPECIMEN PROCESSING**	
AUTHOR:	ISSUE DATE: **March-92**
REVISED BY: **Sharon Bodmer and Kathy Parker**	REVISION DATE: **June-02**

1.0   PURPOSE

   1.1   To ensure all specimens are processed in a standardized consistent manner throughout the AFHS.

2.0   SCOPE

   2.1   Applies to medical laboratory assistants who process blood and urine specimens for the AFHS.

3.0   MATERIALS

   3.1   60-mL (2-oz.) glass jar (provided by AF)
   3.2   1.8-mL nunc vial (provided by AF)
   3.3   Test tubes
   3.4   Electric pipetter
   3.5   Disposable pipettes (provided by AF)
   3.6   Test tube racks
   3.7   Caps for aliquot tubes
   3.8   13 x 100 mm aliquot tubes
   3.9   1.0-mL nunc vials
   3.10   Clear protective tape
   3.11   Centrifuge
   3.12   Scale
   3.13   Ziplock freezer bags
   3.14   Wipes

4.0   PROCEDURE

   4.1   Processing will begin when the first specimens are drawn at approximately 0645 day 1.
   4.2   Serum specimens should be allowed to clot for a minimum of 15 minutes.
   4.3   Specimens that need to be centrifuged should be balanced and centrifuged at 3,000 revolutions per minute at 2 to 8 °C for 10 minutes.
   4.4   Fasting first-morning urines will be collected from all participants on day 1 at their hotel.

        4.4.1   Specimen processors will aliquot urines from screw-cap collection cups into one KOVA tube and one urine collection tube.

        4.4.2   Place one KOVA tube in test tube rack labeled **Air Force UA.** Place the urine collection tube in test tube rack labeled **Air Force MA**. Deliver the **Air Force UA** to hematology and deliver the **Air Force MA** to chemistry once all fasting urines are aliquoted.

4.5   One lavender tube of blood labeled **AFCBCC**, **AFCBCD**, and **AFESR** will be drawn and placed in a test tube rack labeled **Air Force Hematology**.

        4.5.1   These specimens will be delivered to hematology once they are all drawn, along with their aliquot labels (**AFCBCC**) and two slide labels.

        4.5.2   These specimens will be kept at room temperature until delivery.

4.6   One blue (citrate) tube of blood labeled **AFPTP and AFFIB** will be drawn and placed in a test tube rack labeled **Air Force Coagulation.**

        4.6.1   This specimen will be delivered to coagulation once it is drawn.

        4.6.2   These specimens will be kept at room temperature until delivery.

4.7   One lavender tube of blood labeled **AFTCEL** will be drawn and placed in a test tube rack labeled **Air Force TCEL.**

        4.7.1   These specimens will be delivered to flow cytometry once they are drawn.

4.8   It is essential that these specimens remain at room temperature from draw time until delivery.

4.9   One 7-mL SST tube of blood labeled **AFCHEM** will be drawn and placed in a rack labeled **Air Force Chemistry.**

        4.9.1   Once clotted, these tubes will be centrifuged first.

        4.9.2   Once centrifuged, these tubes will be returned to the rack labeled **Air Force Chemistry** and delivered to a designated bench in Chemistry.

4.10   Four 7-mL SST tubes labeled **AFPRPF** and **AFRIA** will be drawn and placed in a rack labeled **Air Force PRPF & RIA**.

        4.10.1   Once clotted, these tubes will be centrifuged.

        4.10.2   Once centrifuged, these tubes will be returned to the rack labeled **Air Force PRPF & RIA** and delivered to a designated bench in Chemistry.

4.11   Two 7-mL SST tubes of blood labeled **AFLP** and **AFTH** will be drawn and placed in a rack labeled **Air Force LP&TH**.

        4.11.1   Once clotted, these tubes will be centrifuged.

        4.11.2   Once centrifuged, these tubes will be returned to the rack labeled **Air Force LP&TH** and delivered to a designated bench in Chemistry.

4.12   One 4-mL SST tube labeled **AFHA** will be drawn and placed in a rack labeled **Air Force HA.**

        4.12.1   Once clotted, these tubes will be centrifuged.

        4.12.2   Once centrifuged, these tubes will be returned to the rack labeled **Air Force HA** and delivered to a designated bench in Chemistry.

4.13   One 7-mL SST, one 10-mL plain red-top, and one lavender tube of blood labeled **AFDIA** will be drawn for diabetic testing and placed in three racks labeled **Air Force DIA (Lavender), Air Force DIA (SST 7 mL), and Air Force DIA (Plain Red 10 mL).**

        4.13.1   Once the 7-mL SST and the plain red-top tubes are clotted, they will be centrifuged. The lavender tube should not be centrifuged.

        4.13.2   Once the 7-mL SST tube is centrifuged it will be returned to a rack labeled **Air Force DIA (SST 7 mL)** and delivered to a designated bench in Chemistry.

        4.13.3   The lavender tube should also be delivered to a designated bench in Chemistry.

        4.13.4   Once centrifuged the 10-mL plain red-top tube must be aliquoted into two aliquot tubes and placed into the three racks labeled **Air Force Proinsulin, Air Force Proinsulin Unknown, and Air Force Proinsulin Save.** Fill out sendout paperwork for the Air Force Proinsulin tests and place each specimen and requisition into a ziplock freezer bag.

4.14   One yellow tube of blood labeled **AFW** will be drawn for archive, kept at room temperature, and placed in a rack labeled **Air Force Whole Blood (Yellow)**.

        4.14.1   Gently agitate tube by hand two times immediately after blood is drawn. Label each of the 10 nunc vials with slide labels. Mix well just before pipetting into nunc vials.

        4.14.2   Cover label on nunc vial with clear protective tape.

        4.14.3   Pipette 1 mL into each of nine 1.2 nunc vials with the remainder of blood going into the tenth vial.

        4.14.4   Place in nunc tube box and freeze at -70 °C.

4.15   Six 10-mL plain red-top and one 4-mL lavender tubes (furnished by the Air Force) of blood labeled **AFX** will be drawn on all participants for dioxin testing and placed in a rack labeled **Air Force Dioxin.**

        4.15.1   Once clotted (approximately 20 to 30 minutes), centrifuge all specimens for 15 minutes.

        4.15.2   Label one 1.8-mL nunc vial (furnished by the Air Force) with a slide label. Cover the label of the nunc vial using clear protective tape. Pipette 1.8 mL of plasma from lavender top tube and transfer it into the 1.8-mL prelabeled nunc vial (furnished by the Air Force).

        4.15.3   Label the 60-mL (2-oz.) glass jar furnished by the Air Force with **TRANS1** aliquot label. Initial this label. Cover the label with clear protective tape.

        4.15.4   Transfer all serum from the six red-top tubes into the glass jar. Any serum that has become mixed must be transferred into a clean 10-mL red-top tube and recentrifuged. If tubes are recentrifuged, transfer remaining serum into glass jar.

        4.15.5   Replace the Teflon-lined, green screw cap and freeze.

        4.15.6   Place upright in a -70 °C freezer and store at the same temperature until shipment to Brooks City-Base.

4.16   Eight 10-mL SST tubes labeled **AFSAVE** will be drawn for serum storage and placed in a rack labeled **Air Force SAVE**.

        4.16.1   Once clotted, these tubes will be centrifuged.

        4.16.2   Once centrifuged, these tubes will be matched up with four previously labeled Mylar®-covered aliquot tubes (three 13 x 100 mm and one small aliquot tube).

        4.16.3   Serum in amounts on label for **Air Force SAVE** will be aliquoted into the tubes prelabeled as follows:
             SAV10A
             SAV10B
             SAV10C
             SAV5D.

        4.16.4   Once aliquoted, these specimens will be placed in a rack labeled **Air Force SAVE** (keeping all four tubes together). Rack will be placed in a designated -70 °C freezer for storage until shipped to Brooks City-Base.

4.17   One 4-mL SST tube of blood labeled **AF2HIN** will be drawn for 2-hour postprandial glucose and insulin level and placed in a rack labeled **Air Force 2HIN**.

4.17.1   Once clotted, these tubes will be centrifuged.

4.17.2   Once centrifuged, these tubes will be returned to the rack labeled **Air Force 2HIN** and delivered to a designated bench in Chemistry.

5.0   Urines for 2-hour postprandial glucose will be collected in screw-cap collection cups. Specimen processor will pour urine into KOVA tube and place in the rack labeled **Air Force 2HUR** and delivered to a designated bench in Hematology.

6.0   Blood tubes that have been aliquoted will be stored in the specimen processing freezer for 2 days.

7.0   Restock and inventory all supplies.

POLICIES AND PROCEDURES

Scripps Clinic
Department of Pathology (211C)
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LABORATORY SECTION: **SPECIMEN PROCESSING**	
TITLE: **AFHS - SHIPPING SPECIMENS TO BROOKS CITY-BASE**	
AUTHOR:	ISSUE DATE: **April-92**
REVISED BY: **Sharon Bodmer & Kathy Parker**	REVISION DATE: **April-02**

1.0   PURPOSE:

    1.1   To ensure the consistent packaging and shipping of all specimens to Brooks City-Base.

2.0   SCOPE:
    2.1   Applies to all medical laboratory assistants who pack and ship specimens for the Air
           Force Health Study (AFHS).

3.0   PROCEDURE

    3.1   Serum for dioxin labeled **TRANS1,** serum for archive labeled **SAVE,** 10 1-mL nunc
           vials of whole blood for archive, and 1 1.8-mL nunc vial of serum for lipid studies will be
           shipped twice a week to Brooks City-Base.
    3.2   Specimens will be shipped Tuesdays and Thursdays and include all specimens from that
           week.
    3.3   Each participant should have 4 serum aliquots, 10 whole blood aliquots, 1 60-mL (2-oz.)
           glass jar of serum for dioxin, and 1 1.8-mL nunc vial unless specimens were unattainable.
           3.3.1   If specimens were unattainable, indicate on participant group list the reason for
                  reduced number of specimens or lack of specimens (i.e., no show, short draw,
                  patient refused).
    3.4   Specimens will be stored at -70 °C until shipped.
           3.4.1   On Tuesdays and Thursdays, all specimens obtained from the previous day's
                  participants will be shipped.
                  3.4.1.1   As each participant's specimens are packed for shipping, check off the
                        name of the participant on the participant group list. This will become
                        the participant shipping list. When completed, fax this participant
                        shipping list to Brooks City-Base, attention Vince Elequin at (210)
                        536-3567. Make a copy of the shipping list and give to Sharon Bodmer.
                        Send original copy of shipping list with specimens.
           3.4.2   Once all specimens are packed, add a sufficient amount of dry ice (approximately
                  15 lbs.) on top of the specimens to keep them frozen during overnight shipment.
                  Buffer with additional bubble pack as needed. Seal the Styrofoam® container
                  with tape.
           3.4.3   Put the participant shipping list in a ziplock bag and place the bag on top of the
                  Styrofoam container inside the shipping box. Close the shipping box and seal
                  with strapping tape.
           3.4.4   Specimens will be mailed via FedEx® overnight mail.

Fill out the overnight mail slip as follows:

Deputy Chief, Air Force Health Study
AFRL/HEDA
2655 Flight Nurse, Bldg 807
Brooks City-Base, TX 78235-5137
ATTN: Vince Elequin

This will be billed to acct. #20-227-7530.

3.4.5   Take all shipping boxes to shipping department before 1430 on Tuesdays and Thursdays.

This appendix contains the following items:

1. The Examiners' Handbook *
2. The data collection forms.

The Examiners' Handbook presented here is as it appeared in the Air Force Health Study Statement of Work dated 27 August 2001 with updates through 31 January 2002. Some minor changes and procedural modifications were made prior to the commencement of the physical examinations and are not reflected here.

ADDENDUM A

STATEMENT OF WORK

FOR THE

AIR FORCE HEALTH STUDY

2002 FOLLOW-UP EXAMINATION

AIR FORCE HEALTH STUDY
EXAMINERS HANDBOOK

31 January 2002

Air Force Health Study Examiner's Handbook

A. General Instructions

The Air Force Health Study is a multiyear prospective study to determine whether Air Force personnel who were engaged with spraying herbicides in Vietnam have developed adverse health effects from exposure to herbicides and their contaminant, 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin). Detailed surveys of the scientific literature have been used to design the questionnaires, the physical examination protocol and select laboratory tests.

This phase of the study involves a follow-up cross-sectional assessment of each subject's health at the time of the examination. It is important that examiners remain unaware of the subject's exposure status (Ranch Hand, Comparison). The physician examiner is tasked to examine each subject and objectively record findings. The examining physician is not, and cannot be expected to arrive at any definitive diagnoses, since the full history and physical examination findings and laboratory results shall not be available. An independent diagnostician employed by the contractor shall evaluate medical history, laboratory results and physical examination findings. The diagnostician shall formulate diagnoses and differential diagnoses, if appropriate. Additional procedures to treat or evaluate emergency or urgent medical conditions shall be directed only by the diagnostician. In addition, the diagnostician shall present a detailed analysis and debriefing to each study subject and provide a copy of the analysis for the subject's personal physician, if authorized by the subject.

The physicians performing examinations for the study should be aware that the report of the examination will become a permanent record. The report shall be referenced not only in the near future as the cross-sectional data is analyzed, but also during future follow-up phases of the study. These examinations shall define the health status of the subjects at a point in time and shall establish the presence or absence of abnormal physical findings. After statistical review of the study groups, these findings may permit definition of chronic or latent effects due to exposure. An inaccurate examination may lead to fallacious results in two ways: a presumed syndrome may be defined which does not in fact exist, or a syndrome which in fact exists may not be defined with enough validity to warrant further action.

The examining physician is responsible for recording a complete and detailed report of the physical examination. The examining physician shall fill out all forms and check the forms for completeness and logical consistency before the patient leaves the examining room. In this role, the examining physician is tasked with collecting evidence of the presence or absence of physical signs of abnormality only. All items on the physical examination report form must be completed. It is imperative that physicians make such additional remarks as may be required to adequately describe existing physical abnormalities. Since clinical endpoints have not been well-defined following exposure to Agent Orange, the examining physician and the diagnostician must not definitively ascribe abnormalities to herbicide exposure during the course of the examination or during the debriefings. If, during the examination, the physician discovers evidence of acute serious illness requiring immediate treatment, the normal emergency or urgent care procedure of the medical facility would apply. The Air Force is not responsible for the cost of such emergency or urgent care.

The debriefing physician shall ask each participant if he received additional testing or additional medical treatment during the physical examination time period and shall annotate any such circumstances or results on the debriefing form. The ultimate value of the study will lie in the collection of complete, accurate and, whenever possible, quantitative data permitting the most stringent and powerful statistical analysis. For this reason, the physical examination protocol requires, whenever possible, exact measurements and well defined semi-quantitative indicators of abnormalities.

B. Conduct of the Examination

1. OVERVIEW

Upon arrival at the examining facility, a representative of the contractor on the nature, time and location of each appointment shall brief the subject. Consent forms covering all examination procedures will be provided to each subject. The subject may decline to participate in any individual portion of the examination, even if he previously signed a consent form. The examination shall be conducted in a manner identical to that used in prior phases of the study and in accord with detail in subsequent sections of this handbook and the Statement of Work.

2. GENERAL PHYSICAL EXAMINATION

The general physical examination shall include an assessment of

1. Appearance (well nourished, obese, under nourished),
2. Appearance relative to stated age (same as, older than, younger than),
3. Appearance of illness or distress (no, yes),
4. Hair distribution (normal, abnormal),
5. Vital signs (height in centimeters, weight undressed in kilograms, oral temperature),
6. Systolic and diastolic blood pressure,
7. Pulse rate,
8. An eye examination (fundoscopic and external observation),
9. An ENT/neck examination,
10. A thorax and lung examination,
11. Waist, hip, chest and neck measurements in centimeters,
12. A heart examination including an overall diagnosis (normal, abnormal, refused),
13. An examination of the abdomen, extremities and peripheral pulses, musculature and spine,
14. An examination of the genitourinary system,
15. A rectal examination,
16. An assessment of the lymph nodes (normal, enlarged, tender, hard, fixed, confluent, other), and
17. A summary of follow-up indicated or recommended.

3. DERMATOLOGIC EXAMINATION AND BIOPSY

The examination shall include

1. An examination of the skin,
2. Skin biopsy, if indicated,
3. Physical features, and
4. Mapping of lesions on an anatomical chart.

4. NEUROLOGICAL EXAMINATION

The examination shall include

1. An examination of the head and neck,
2. An examination of motor systems,
3. An examination of muscle status,
4. An assessment of abnormal movements,
5. An assessment of tremors,
6. An assessment of coordination,
7. An assessment of deep tendon reflexes,
8. An assessment of cranial nerves and mental status,
9. An assessment of meningeal irritation and sensory system,
10. An examination of cranial nerves (I, VII),
11. An examination of cranial nerves (II),
12. An examination of cranial nerves (III, IV, VI),
13. An examination of cranial nerves (V, IX, XI, XII),
14. An impression of the entire neurological examination,
15. Measurement of nerve conduction velocities.

5. PSYCHOLOGICAL TESTING

The Symptom Check List 90-Revised (SCL90R) and Wechsler Memory Scale [Version 1] shall be administered to all study subjects. These tests were chosen to ensure adequate analysis of possible psychological and cognitive manifestations of herbicide toxicity. The psychologist in charge will interpret the results of the test, record those interpretations on a form and provide them to the debriefing physician. The contractor shall forward all test materials as scored with annotations, interpretations and impressions to the diagnostician for inclusion in the subject's file.

6. ELECTROCARDIOGRAM

A standard 12-lead scalar electrocardiogram is required. If an arrhythmia is observed, a 1-minute rhythm strip is additionally requested. This electrocardiogram will be accomplished after a test-specific abstinence from smoking, food and liquid intake. The tracing shall be mounted in the usual manner of the laboratory for the recorder used. Cardiologists at the examination facility will interpret the electrocardiograms. The cardiologist shall forward the interpretation, mounted tracing and rhythm strip, if obtained, to the diagnostician.

7. PULMONARY FUNCTION TESTING

Standard evaluation of pulmonary function will be conducted on each subject following a test-specific abstention from the use of tobacco products and will include, as minimum, forced expiratory volume at 1 second, total vital capacity, and the ratio of the two measurements.

8. AUTOMATED BLOOD PRESSURE DETERMINATION

An electronic device will be used to measure blood pressure. The device to be used will be selected by the contractor, subject to approval by the Air Force.

9. STOOL EXAMINATION FOR OCCULT BLOOD

Three stool smears from each subject will be tested for the presence of occult blood. Subjects with positive tests will be advised and appropriate follow-up will be recommended.

10. RADIOGRAPHIC EXAMINATION

A standard 14×17 inch, standing, roentgenogram in the PA position will be administered to all subjects. A board-certified radiologist at the examining facility will interpret the roentgenogram, record the results and forward them to the diagnostician.

11. DOPPLER TESTING OF PERIPHERAL PULSES

A Doppler device shall be used to quantitatively measure peripheral pulses. Peripheral blood pressures shall be measured. These procedures shall be conducted after a test-specific abstinence from smoking and caffeine.

12. MEASUREMENT OF HEIGHT, WEIGHT, WAIST, HIP, TEMPERATURE

The contractor shall determine the height in centimeters and weight in kilograms following a standard protocol on each subject. The contractor shall also measure the circumference of the waist at the navel, hip, and the circumference of the neck in centimeters. The contractor shall measure temperature in degrees Fahrenheit.

13. LABORATORY PROCEDURES - GENERAL INSTRUCTIONS

On the first day, the subject should report in the morning in a fasting state having had only water after midnight. Blood for the serum dioxin measurement will be drawn on subjects who consent to this procedure. Sufficient blood for the dioxin measurement will be drawn to bring the total volume collected over the 2 days to not more than 450 cc from these volunteers. All study subjects shall be informed that they should abstain from alcohol for 24 hours prior to the start of the physical examination. The contractor shall propose as part of the Biomedical Test Plan, the specific times for abstention requirements of any tests needing abstentions from caffeine, nicotine, food or liquid intake. The ADA fasting glucose criteria shall be used to identify new diabetics.

14. LABORATORY PROCEDURES - SPECIFIC TESTS TO BE PERFORMED

1. α-1-C hemoglobin (percent) (diabetics only)
2. Absolute basophils (thousand/cu mm)
3. Absolute eosinophils (thousand/cu mm)
4. Absolute lymphocytes (thousand/cu mm)
5. Absolute monocytes (thousand/cu mm)
6. Absolute neutrophils (bands) (thousand/cu mm)
7. Absolute neutrophils (segs) (thousand/cu mm)
8. Alkaline phosphatase (U/L)
9. ALT (U/L)
10. Antibodies for hepatitis A (present, absent)
11. Anti-thyroid antibodies (present, absent)
12. AST (U/L)
13. Blood urea nitrogen (mg/dl)
14. CD16+CD56+ (cells/cu mm and percent)
15. CD20 (cells/cu mm and percent)
16. CD3 (cells/cu mm and percent)
17. CD3 + CD4+ (cells/cu mm and percent)
18. CD4 (cells/cu mm and percent)
19. CD45+/CD14+ (%) [quality control marker]
20. CD8 (cells/cu mm and percent)
21. Cholesterol (mg/dl)
22. C-peptide (ng/ml) [diabetics only]
23. Creatine phosphokinase (U/L)
24. Direct bilirubin (mg/dl)
25. Erythrocyte sedimentation rate (mm/hr)
26. Estradiol (pg/ml)
27. Fasting glucose (mg/dl)
28. Fibrinogen (mg/dl)
29. Follicle stimulating hormone (mIU/ml)
30. Free testosterone (pg/ml)
31. GGT (U/L)
32. Glutamic acid decarboxylase antibodies (presence, absence) [diabetic only]
33. HDL cholesterol (mg/dl)
34. Hematocrit (percent)
35. Hemoglobin (gm/dl)
36. IgA (mg/dl)
37. IgG (mg/dl)
38. IgM (mg/dl)
39. Islet cell antibodies (presence, absence) [diabetic only]
40. Lactate dehydrogenase (U/L)
41. Lupus panel: ANA test (presence, absence)
42. Lupus panel: ANA thyroid microsomal antibody (presence, absence)
43. Lupus panel: MSK mitrochondrial antibody (presence, absence)
44. Lupus panel: MSK parietal antibody (presence, absence)

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45. Lupus panel: MSK smooth muscle antibody (presence, absence)
46. Lupus panel: Rheumatoid factor
47. Luteinizing hormone (mIU/ml)
48. Microalbumin (mg/dl)
49. Platelet count (thousand/cu mm)
50. Proinsulin (ng/ml) [diabetics only]
51. Prostate specific antigen (ng/ml)
52. Protein profile: α-1-antitrypsin (mg/dl)
53. Protein profile: α-1-glycoprotein (mg/dl)
54. Protein profile: α-2-macroglobulin (mg/dl)
55. Protein profile: albumin (mg/dl)
56. Protein profile: apolipoprotein (mg/dl)
57. Protein profile: C3 complement (mg/dl)
58. Protein profile: C4 compliment (mg/dl)
59. Protein profile: haptoglobin (mg/dl)
60. Protein profile: pre-albumin (mg/dl)
61. Protein profile: transferrin (mg/dl)
62. Prothrombin time (seconds)
63. RBC morphology (abnormal, normal)
64. Red blood cell count (million/cu mm)
65. Serum amylase (U/L)
66. Serum creatinine (mg/dl)
67. Serum insulin (μIU/ml) (2 hr. pp, non-diabetics only)
68. Serum insulin (μIU/ml) (fasting)
69. Thyroid stimulating hormone (μIU/ml)
70. Thyroid T_3 (low TSH, normal T_4)
71. Thyroid T_4 (μg/dl) (free)
72. Total bilirubin (mg/dl)
73. Total testosterone (ng/dl)
74. Triglycerides (mg/dl)
75. Two-hour postprandial glucose (mg/dl) (non-diabetics only)
76. Two-hour postprandial urinary glucose (present, absent) (non-diabetics only)
77. Uric Acid (mg/dl)
78. Urinary occult blood (RBC/HPF)
79. Urinary creatinine
80. Urinary protein (present, absent)
81. Urine specific gravity
82. Urine white blood cell count (WBC/HPF)
83. White blood cell count (thousand/cu mm)

FORM AFHS-3A PHYSICAL EXAMINATION (PART 1) (SHEET 1 OF 2)

EXAMINER I.D.

YEAR 20 FOLLOW UP

(Y) (N) IS PARTICIPANT TAKING SYSTEMIC CORTICOSTEROIDS OR IMMUNOSUPPRESSANTS?
SPECIFY MEDICATION(S), DOSAGE(S) & FUNCTION(S) BELOW:

VITAL SIGNS

HEIGHT CM	WEIGHT (LT.DRESS) KG	TEMPERATURE ORAL °F	SITTING BLOOD PRESSURE NONDOMINANT ARM, HEART LEVEL SYSTOLIC	DIASTOLIC	PULSE RATE

(Y) (N) COMMENTS?

(Y) (N) COMPLIANCE TO DIET FOR STOOL SAMPLES?

GENERAL PHYSICAL APPEARANCE

APPEARANCE	APPEARANCE VS STATED AGE	APPEARANCE OF ILLNESS OR DISTRESS	HAIR DISTRIBUTION
○ WELL NOURISHED	○ SAME AS	○ NO	○ NORMAL
○ OBESE	○ OLDER THAN		
○ UNDER NOURISHED	○ YOUNGER THAN	○ YES	○ ABNORMAL

(Y) (N) COMMENTS?

EYES

SUMMARY

○ NORMAL

○ ABNORMAL

○ REFUSED

○ LEFT EYE ABSENT
○ RIGHT EYE ABSENT

FUNDUSCOPIC EXAM

YES	NO		YES	NO	
(Y)	(N) ↑ LIGHT REFLEX		(Y)	(N) HEMORRHAGES	
(Y)	(N) A-V NICKING		(Y)	(N) EXUDATES	
(Y)	(N) ARTERIOLAR SPASM		(Y)	(N) DISK PALLOR	
(Y)	(N) PAPILLEDEMA		(Y)	(N) ↑ CUPPING	
(B)(L)(R)(N) FUNDI WERE VISUALIZED			(Y)	(N) DIABETIC RETINOPATHY	

(B = BOTH, L = LEFT ONLY, R = RIGHT ONLY, N = NEITHER)

EXTERNAL OBSERVATION

YES	NO	
(Y)	(N) ARCUS SENILIS PRESENT	
(Y)	(N) SCLERA PIGMENTATION	

PHYSICIAN'S PRINTED NAME

DATE:

(Y) (N) COMMENTS?

FORM QA AUDIT BY:
(1)(2)(3)(4)(5)(6) INITIALS:

DATE:

Mark Reflex® forms by NCS Pearson   MW211961-3   654321   GS99   Printed in U.S.A.

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER

CASE NUMBER (columns of): ⓪①②③④⑤⑥⑦⑧⑨ (×6 rows)

GROUP NUMBER: ⓪①②③④⑤⑥⑦⑧⑨ (×2 rows)

EXAMINER I.D.: ⓪①②③④⑤⑥⑦⑧⑨ (×3 rows)

UNITED STATES AIR FORCE HEALTH STUDY

YEAR 20 FOLLOW UP

FORM AFHS-3A PHYSICAL EXAMINATION (PART 1) (SHEET 2 OF 2)

Ⓝ = NO OR NONE Ⓨ = YES

Ⓡ = REFUSED Ⓧ = COULD NOT EXAMINE

Ⓛ = LEFT Ⓡ = RIGHT

ENT/NECK

ENT ARE

○ NORMAL
○ ABNORMAL
○ REFUSED

Ⓨ Ⓝ COMMENTS?

	LEFT	RIGHT
TYMPANIC MEMBRANE INTACT?	Ⓨ Ⓝ Ⓧ	Ⓨ Ⓝ Ⓧ
EAR IRRIGATED TO REMOVE WAX?	Ⓝ Ⓨ	Ⓝ Ⓨ
NASAL MUCOSA ULCERATED?	Ⓝ Ⓨ Ⓧ	Ⓝ Ⓨ Ⓧ

	LEFT	RIGHT
PAROTID GLAND ENLARGED?	Ⓝ Ⓨ	Ⓝ Ⓨ
CAROTID BRUIT PRESENT?	Ⓝ Ⓨ	Ⓝ Ⓨ
CAROTID PLUSE IS:	Ⓝ Ⓓ Ⓐ	Ⓝ Ⓓ Ⓐ

○ NORMAL
○ ABNORMAL
○ REFUSED

(N = NORMAL D = DIMINISHED A = ABSENT

○ NORMAL
○ ABNORMAL

THYROID GLAND	ENLARGED		NODULES		TENDER		OTHER	
	Ⓝ	Ⓨ	Ⓝ	Ⓨ	Ⓝ	Ⓨ	Ⓝ	Ⓨ

Ⓨ Ⓝ COMMENTS?

THORAX AND LUNGS

○ NORMAL
○ ABNORMAL
○ REFUSED

Ⓨ Ⓝ COMMENTS?

Ⓨ Ⓝ ASYMMETRICAL EXPANSION

Ⓨ Ⓝ HYPERRESONANCE

Ⓨ Ⓝ DULLNESS

Ⓨ Ⓝ WHEEZES

Ⓨ Ⓝ RALES
← (NOTE LOCATION)
Ⓨ Ⓝ SUSPECTED COPD
← (DESCRIBED)

CIRCUMFERENCE (CM)

WAIST	CHEST AT NIPPLE LEVEL		NECK	HIPS
	INSPIRATION	EXPIRATION		

Digit columns (each 0–9):

WAIST: ⓪①②③④⑤⑥⑦⑧⑨ ⓪①②③④⑤⑥⑦⑧⑨ ⓪①②③④⑤⑥⑦⑧⑨

CHEST INSPIRATION: ⓪①②③④⑤⑥⑦⑧⑨ ⓪①②③④⑤⑥⑦⑧⑨ ⓪①②③④⑤⑥⑦⑧⑨

CHEST EXPIRATION: ⓪①②③④⑤⑥⑦⑧⑨ ⓪①②③④⑤⑥⑦⑧⑨ ⓪①②③④⑤⑥⑦⑧⑨

NECK: ⓪①②③④⑤⑥⑦⑧⑨ ⓪①②③④⑤⑥⑦⑧⑨ ⓪①②③④⑤⑥⑦⑧⑨

HIPS: ⓪①②③④⑤⑥⑦⑧⑨ ⓪①②③④⑤⑥⑦⑧⑨ ⓪①②③④⑤⑥⑦⑧⑨

HEART

HEART EXAM IS:
○ NORMAL
○ ABNORMAL
○ REFUSED

MURMUR?
○ NO
○ YES, PROBABLY FUNCTIONAL
○ YES, SUSPECT ORGANIC
○ YES, ORGANIC

INDICATE CHEST AREA(S) TO WHICH MURMUR WAS PROJECTED MOST INTENSELY.

(MARK Ns IF NO MURMUR)

	S1		S2		S3		S4	
ABNORMAL HEART SOUNDS?	Ⓝ	Ⓨ	Ⓝ	Ⓨ	Ⓝ	Ⓨ	Ⓝ	Ⓨ

Ⓨ Ⓝ DISPLACED APICAL IMPULSE?

Ⓨ Ⓝ PRECORDIAL THRUST?

	SYSTOLIC		DIASTOLIC	
AORTIC	Ⓝ	Ⓨ	Ⓝ	Ⓨ
PULMONIC	Ⓝ	Ⓨ	Ⓝ	Ⓨ
APEX	Ⓝ	Ⓨ	Ⓝ	Ⓨ
LLSB	Ⓝ	Ⓨ	Ⓝ	Ⓨ

Ⓨ Ⓝ HEART COMMENTS?

FORM QA AUDIT BY:
① ② ③ ④ ⑤ ⑥ INITIALS:

DATE:

B-10

CASE NUMBER
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨

GROUP NUMBER
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨

EXAMINER I.D.
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨

UNITED STATES AIR FORCE HEALTH STUDY

YEAR 20 FOLLOW UP

FORM AFHS-3B PHYSICAL EXAMINATION (PART 2) (SHEET 1 OF 2)

ABDOMEN

(Y) (N) ABDOMEN COMMENTS?

	YES	NO	
	○	○	HEPATOMEGALY
○ NORMAL	○	○	LIVER TENDERNESS
○ ABNORMAL	○	○	SPLENOMEGALY
○ REFUSED	○	○	SPLEEN TENDERNESS
	○	○	OTHER MASS? ⟶

TOTAL LIVER SPAN
⓪①②③④ CM
⓪①②③④⑤⑥⑦⑧⑨

(Y) (N) COMMENTS, MASS SIZE (CM), LOCATION, TYPE

EXTREMITIES

	AMPUTATION(S)	PITTING EDEMA	NON-PITTING EDEMA	CLUBBED NAILS	VARICOSITIES	
UPPER LIMBS	(N)(L)(R)	(N)(L)(R)	(N)(L)(R)	(N)(L)(R)	(N)(L)(R)	

(N = NONE OR NORMAL FOR BOTH LIMBS, L = LEFT LIMB ONLY, R = RIGHT LIMB ONLY)

TOE HAIR LOSS

| LOWER LIMBS | (N)(L)(R) | (N)(L)(R) | (N)(L)(R) | (N)(L)(R) | (N)(L)(R) | (N)(L)(R) |

EXTREMITY EXAM WAS: ○ NORMAL   ○ ABNORMAL   ○ REFUSED

(Y) (N) DESCRIBE ABSENCES & / OR ABNORMALITIES

PERIPHERAL PULSES

(N)(L)(R) FEMORAL BRUIT(S) PRESENT?
(N = NONE, L = LEFT, R = RIGHT)

	RADIAL		FEMORAL		POPLITEAL		DORSALIS PEDIS		POSTERIOR TIBIAL	
	LEFT	RIGHT	LEFT	RIGHT	LEFT	RIGHT	LEFT	RIGHT	LEFT	RIGHT
NORMAL	○	○	○	○	○	○	○	○	○	○
DIMINISHED	○	○	○	○	○	○	○	○	○	○
ABSENT	○	○	○	○	○	○	○	○	○	○
COULD NOT EXAMINE	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)

(Y) (N) PULSE COMMENTS

MUSCULATURE

		NO	YES	CNE
○ NORMAL	STRAIGHT LEG RAISE ABNORMAL?	○	○	(X)
○ ABNORMAL	ANY WEAKNESS NOTED?	○	○	(X)
○ REFUSED	ANY TENDERNESS NOTED?	○	○	(X)
	ANY ATROPHY NOTED?	○	○	(X)
	ABNORMAL CONSISTENCY?	○	○	(X)
	OTHER ABNORMALITY?	○	○	(X)

(Y) (N) COMMENTS?

SPINE

		NO	YES	CNE	SPINAL TENDERNESS
○ NORMAL	ANY SCOLIOSIS NOTED?	○	○	(X)	○ NONE NOTED
○ ABNORMAL	ANY KYPHOSIS NOTED?	○	○	(X)	○ CERVICAL AREA
○ REFUSED	PELVIC TILT NOTED?	○	○	(X)	○ THORACIC AREA
	↓ RANGE OF MOTION?	○	○	(X)	○ LUMBAR AREA
					○ SACRAL AREA

(Y) (N) COMMENTS?

FORM QA AUDIT BY:
① ② ③ ④ ⑤ ⑥ INITIALS:

DATE:

PARTICIPANT LABEL

CASE NUMBER
⓪①②③④⑤⑥⑦⑧⑨
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GROUP NUMBER
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨

EXAMINER I.D.
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨
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UNITED STATES AIR FORCE
HEALTH STUDY

YEAR 20 FOLLOW UP

FORM AFHS-3B PHYSICAL EXAMINATION (PART 2) (SHEET 2 OF 2)

GENITOURINARY EXAM
(PE PART 2 CONTINUED)

GENITOURINARY EXAM
○ NORMAL
○ ABNORMAL
○ REFUSED

TESTES

	NORMAL	ENLARGED	NODULE	ATROPHIC	ABSENT	OTHER
LEFT	○	○	○	○	○	○
RIGHT	○	○	○	○	○	○

YES	NO	REFUSED	
Ⓨ	Ⓝ	Ⓡ	RIGHT INGUINAL HERNIA?
Ⓨ	Ⓝ	Ⓡ	LEFT INGUINAL HERNIA?
Ⓨ	Ⓝ	Ⓡ	SCROTAL MASS PRESENT?

YES	NO	REFUSED	
Ⓨ	Ⓝ	Ⓡ	VARICOCELE
Ⓨ	Ⓝ	Ⓡ	EPIDIDYMAL ABNORMALITY

⓪①②③④⑤⑥⑦⑧⊕ SCROTAL MASS SIZE (DIAMETER IN CM)

Ⓨ Ⓝ COMMENTS:

RECTAL EXAM

RECTAL EXAM
○ NORMAL
○ ABNORMAL
○ REFUSED

HEMORRHOIDS	NONE APPARENT	REFUSED	BLEEDING	THROMBOSED	OTHER
EXTERNAL	○	○	○	○	○
INTERNAL	○	○	○	○	○

YES	NO	REFUSED	
○	○	○	PROSTATIC ENLARGEMENT?
○	○	○	RECTAL MASS (ES)?

Ⓨ Ⓝ COMMENTS:

LYMPH NODES

VARIATIONS FROM NORMAL

○ NORMAL
○ NORMAL WITH NOTED VARIATIONS
○ ABNORMAL

○ REFUSED

	ENLARGED	TENDER	HARD	FIXED	CONFLUENT	OTHER
CERVICAL	○	○	○	○	○	○
OCCIPITAL	○	○	○	○	○	○
SUPRACLAVICULAR	○	○	○	○	○	○
AXILLARY	○	○	○	○	○	○
EPITROCHLEAR	○	○	○	○	○	○
INGUINAL	○	○	○	○	○	○
FEMORAL	○	○	○	○	○	○

Ⓨ Ⓝ COMMENTS:

SUMMARY OF FOLLOW-UP INDICATED OR RECOMMENDED

SUMMARY OF FINDINGS ENTIRE EXAM WAS: ○ ALL NORMAL   ○ ABNORMAL AS SUMMARIZED
○ NORMAL W/NOTED VARIATIONS   ○ REFUSED ENTIRE EXAM

Ⓨ Ⓝ COMMENTS:

PRINTED NAME OF EXAMINING PHYSICIAN	INITIALS / DATE	FORM QA AUDIT BY:
		①②③④⑤⑥ INITIALS:
		DATE:

CASE NUMBER
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UNITED STATES AIR FORCE HEALTH STUDY

YEAR 20 FOLLOW UP

FORM AFHS-4A DERMATOLOGIC EXAMINATION AND BIOPSY

FOR POSITIVE FINDINGS NOTE TYPE AND LOCATION ON ANATOMIC CHART AND DARKEN THE APPROPRIATE CIRCLE BELOW

SKIN

EXAM WAS: ○ NORMAL ○ NORMAL WITH RESULTS ○ ABNORMAL ○ REFUSED | ANATOMICAL CHART USED? Ⓨ Ⓝ

YES	NO	TYPE		YES	NO	TYPE	
○	○	1	COMEDONES	○	○	17	ORAL MUCOSAL ABNORMALITY
○	○	2	ACNEIFORM LESIONS	○	○	18	FINGERNAIL ABNORMALITY
○	○	3	ACNEIFORM SCARS	○	○	19	TOENAIL ABNORMALITY
○	○	4	DEPIGMENTATION	○	○	20	DERMATOGRAPHIA
○	○	5	INCLUSION CYSTS	○	○	21	SUSPECTED BASAL CELL CARCINOMA
○	○	6	CUTIS RHOMBOIDALIS	○	○	22	SUSPECTED SQUAMOUS CELL CARCINOMA
○	○	7	HYPERPIGMENTATION	○	○	23	ATYPICAL/UNUSUAL NEVUS
○	○	8	JAUNDICE	○	○	24	VITILIGO
○	○	9	SPIDER ANGIOMATA	○	○	25	TINEA PEDIS
○	○	10	PALMAR ERYTHEMA	○	○	26	INTERTRIGO
○	○	11	SUSPECTED MELANOMA	○	○	27	LIPOMA
○	○	12	PALMAR KERATOSES	○	○	28	ECZEMA
○	○	13	ACTINIC KERATOSES	○	○	29	PSORIASIS
○	○	14	PETECHIAE	○	○	30	SEBORRHEIC DERMATITIS
○	○	15	ECCHYMOSES	○	○	31	OTHER ABNORMALITY (IES)
○	○	16	CONJUNCTIVAL ABNORMALITY				

SKIN BIOPSY

○ BIOPSY NOT INDICATED → ○ BIOPSY REFUSED → # SAMPLES ①②③④⑤⑥⑦⑧⑨
○ BIOPSY INDICATED, IF SO → ○ BIOPSY PERFORMED, IF SO → YES ○ CONSENT FORM OBTAINED
NO ○

Ⓨ Ⓝ SAMPLE # TYPE AND LOCATION CODE(S) | Ⓨ Ⓝ COMMENT(S)/SUSPECTED DIAGNOSIS

PRINTED NAME OF EXAMINING PHYSICIAN | INITIALS / DATE | FORM QA AUDIT BY: ①②③④⑤⑥ INITIALS:

DATE:

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PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER

CASE NUMBER
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⓪①②③④⑤⑥⑦⑧⑨

UNITED STATES AIR FORCE HEALTH STUDY

YEAR 20 FOLLOW UP

FORM AFHS-4B PHYSICAL FEATURES

Ⓨ Ⓝ Ⓧ WEARING COLORED OR TINTED CONTACTS?

EYE COLOR

	LEFT	RIGHT
BROWN	○	○
HAZEL	○	○
GREEN	○	○
GREY	○	○
BLUE	○	○
ABSENT	○	○

HAIR COLOR

SOLID COLOR ➡ GREYS

BLACKS	① ㉞ ㊹	�51 ⑮
BROWNS	⑤ ⑪ ㊱ ㊳ ㊴ ㊽ �54	
BLONDS	⑭ ⑩③	⑩⑩
REDS	㉝ ㉙	
BALD	⓪	Ⓧ NOT NEEDED

(NOTE: 151 - BLACK AND GREY)

Ⓨ Ⓝ IS HAIR DYED OR ALTERED?

SKIN COLOR

NN
Ⓧ①②③④⑤⑥⑦⑧⑨⑩

Ⓨ Ⓝ COMMENTS?

PRINTED NAME OF EXAMINING PHYSICIAN	INITIALS/DATE	FORM QA AUDIT BY:
		①②③④⑤⑥ INITIALS:
		DATE:

CASE NUMBER	GROUP NUMBER

CASE NUMBER columns (each): (0)(1)(2)(3)(4)(5)(6)(7)(8)(9) — six rows

GROUP NUMBER: (0)(1)(2)(3)(4)(5)(6)(7)(8)(9) — two rows

EXAMINER I.D.

(0)(1)(2)(3)(4)(5)(6)(7)(8)(9) — four rows

UNITED STATES AIR FORCE HEALTH STUDY

YEAR 20 FOLLOW UP

FORM AFHS- 5 NEUROLOGIC EXAMINATION (SHEET 1 OF 3)

HEAD AND NECK

INSPECTION AND PALPATION

○ NORMAL
○ ABNORMAL

	CNE	YES	NO	
	(X)	(Y)	(N)	ASYMMETRY
	(X)	(Y)	(N)	DEPRESSION
	(X)	(Y)	(N)	SCAR
	(X)	(Y)	(N)	OTHER

NECK RANGE OF MOTION

	NORMAL	DECREASED	CNE
LEFT	○	○	(X)
RIGHT	○	○	(X)
FORWARD	○	○	(X)
BACKWARD	○	○	(X)

(Y) (N) COMMENTS

MOTOR SYSTEMS

○ NORMAL
○ ABNORMAL
○ COULD NOT EXAMINE

GAIT
(Y) (N) BROAD BASED
(Y) (N) SMALL STEPPED
(Y) (N) ATAXIC
(Y) (N) OTHER

(Y) (N) COMMENTS

ARM SWING MOVEMENT

	NORMAL	ABNORMAL	CNE
LEFT	○	○	(X)
RIGHT	○	○	(X)

HANDEDNESS

○ LEFT
○ RIGHT
○ BOTH

MUSCLE STATUS

BULK ○ NORMAL ○ ABNORMAL

TONE	NORMAL	CNE	DECREASED LEFT	RIGHT	BOTH	INCREASED LEFT	RIGHT	BOTH
UPPER EXTREMITIES	○	(X)	○	○	○	○	○	○
LOWER EXTREMITIES	○	(X)	○	○	○	○	○	○

STRENGTH	NORMAL	CNE	LEFT	RIGHT	BOTH			
DISTAL WRIST EXTENSORS	○	(X)	○	○	○			
ANKLE/TOE FLEXORS	○	(X)	○	○	○			
PROXIMAL DELTOIDS	○	(X)	○	○	○			
HIP FLEXORS	○	(X)	○	○	○			

(Y) (N) COMMENTS

(Y) (N) TICS, CHOREAS, FASCICULATIONS (1)(2)(3)(4) (Y) (N) TENDERNESS (1)(2)(3)(4) (Y) (N) COMMENTS

TREMOR(S)

EXTREMITY

	UPPER LEFT	UPPER RIGHT	LOWER LEFT	LOWER RIGHT
NO TREMOR	○	○	○	○
RESTING	○	○	○	○
ESSENTIAL	○	○	○	○
INTENTION	○	○	○	○
OTHER	○	○	○	○

(Y) (N) COMMENTS

SPEECH

○ NORMAL ○ DYSARTHRIA
○ APHASIA ○ ANOMIA
○ OTHER ABNORMALITY

(Y) (N) COMMENTS

DEEP TENDON REFLEXES

(0=ABSENT, 1=SLUGGISH, 2=ACTIVE, 3=VERY ACTIVE, X=CNE)

	LEFT ACTIVITY				CNE	RIGHT ACTIVITY				CNE
BICEPS	(0)	(1)	(2)	(3)	(X)	(0)	(1)	(2)	(3)	(X)
TRICEPS	(0)	(1)	(2)	(3)	(X)	(0)	(1)	(2)	(3)	(X)
PATELLAR	(0)	(1)	(2)	(3)	(X)	(0)	(1)	(2)	(3)	(X)
ACHILLES	(0)	(1)	(2)	(3)	(X)	(0)	(1)	(2)	(3)	(X)
BABINSKI	PRESENT ○ ABSENT ○				(X)	PRESENT ○ ABSENT ○				(X)

(Y) (N) COMMENTS

CLONUS

	LEFT ABSENT	UNSUSTAINED	SUSTAINED	CNE	RIGHT ABSENT	UNSUSTAINED	SUSTAINED	CNE
PATELLAR	○	○	○	(X)	○	○	○	(X)
ACHILLES	○	○	○	(X)	○	○	○	(X)

FORM QA AUDIT BY: (1)(2)(3)(4)(5)(6) INITIALS:

DATE:

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
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	⓪①②③④⑤⑥⑦⑧⑨	**EXAMINER I.D.**
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UNITED STATES AIR FORCE HEALTH STUDY

YEAR 20 FOLLOW UP

FORM AFHS-5 NEUROLOGIC EXAMINATION (SHEET 2 OF 3)

COORDINATION

	NORMAL	ABNORMAL	ABNORMAL LEFT	RIGHT	BOTH	CNE	(Y)(N) COMMENTS
1 EQUILIBRIUM (ROMBERG)	○	○				Ⓧ	
2 FINGER-NOSE-FINGER	○		○	○	○	Ⓧ	
3 HEEL-KNEE-SHIN	○		○	○	○	Ⓧ	
4 HAND PRONATION/SUPINATION	○		○	○	○	Ⓧ	
5 RAPID PATTING	○		○	○	○	Ⓧ	

MENINGEAL IRRITATION AND SENSORY SYSTEM

LL = LOWER LIMBS

	NORMAL	-ABNORMAL- LEFT	RIGHT	BOTH	CNE	(Y)(N) COMMENTS
STRAIGHT LEG RAISING	○	○	○	○	Ⓧ	
LIGHT TOUCH (LL)	○	○	○	○	Ⓧ	
PINPRICK (LL)	○	○	○	●	Ⓧ	
VIBRATION AT ANKLE (128 HZ)	○	○	○	●	Ⓧ	
POSITION (GREAT TOE)	○	○	○	○	Ⓧ	

CRANIAL NERVES AND MENTAL STATUS

CODES:
Ⓧ = COULD NOT EXAMINE Ⓝ = NO; NOT NORMAL Ⓨ = YES, NORMAL
Ⓡ = DEVIATED TO RIGHT SIDE Ⓛ = DEVIATED TO LEFT SIDE

CRANIAL NERVES (I, VII)

LEFT	RIGHT		(Y)(N) COMMENTS (I, VII)
ⓍⓃⓎ	ⓍⓃⓎ	SENSE OF SMELL PRESENT?	
ⓍⓃⓎ	ⓍⓃⓎ	SMILE NORMAL?	
ⓍⓃⓎ	ⓍⓃⓎ	PALPEBRAL FISSURE NORMAL?	

CRANIAL NERVES (II)

LEFT	RIGHT		(Y)(N) COMMENTS (II)
ⓍⓃⓎ	ⓍⓃⓎ	FUNDUSCOPIC EXAM NORMAL?	
ⓍⓃⓎ	ⓍⓃⓎ	ABSENCE OF DISK PALLOR/ATROPHY?	
ⓍⓃⓎ	ⓍⓃⓎ	ABSENCE OF PAPILLEDEMA?	
ⓍⓃⓎ	ⓍⓃⓎ	VISUAL FIELDS NORMAL TO CONFRONTATION?	

CRANIAL NERVES (III, IV, VI)

	LEFT	RIGHT	
PUPILS EQUAL SIZE? IF DIFFERENT → ①②③④ mm →		ⓍⓃⓎ	
PUPIL SHAPE/POSITION ROUND & NORMAL?	ⓍⓃⓎ	ⓍⓃⓎ →	DRAW ABNORMAL POSITIONS
LIGHT REACTION NORMAL?	ⓍⓃⓎ	ⓍⓃⓎ	
EYE MOVEMENT NORMAL?	ⓍⓃⓎ	ⓍⓃⓎ	
HORIZONTAL NYSTAGMUS ABSENT?	ⓍⓃⓎ	ⓍⓃⓎ	
VERTICAL NYSTAGMUS ABSENT?	ⓍⓃⓎ	ⓍⓃⓎ	
ROTARY NYSTAGMUS ABSENT?	ⓍⓃⓎ	ⓍⓃⓎ	
EXTRA-OCULAR MOVEMENT INTACT?	ⓍⓃⓎ	ⓍⓃⓎ	
PTOSIS ABSENT?	ⓍⓃⓎ	ⓍⓃⓎ	

(Y)(N) COMMENTS? (III, IV, VI)

FORM QA AUDIT BY:
①②③④⑤⑥ INITIALS:

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CASE NUMBER
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UNITED STATES AIR FORCE HEALTH STUDY

FORM AFHS - 5 NEUROLOGIC EXAMINATION (SHEET 3 OF 3)

YEAR 20 FOLLOW UP

CRANIAL NERVES (V, IX, XI, XII)

LEFT	RIGHT	
(X)(N)(Y)	(X)(N)(Y)	ARE YOU CURRENTLY WEARING CONTACT LENSES?
(X)(N)(Y)	(X)(N)(Y)	CORNEAL REFLEX NORMAL?
(X)(N)(Y)	(X)(N)(Y)	TRIGEMINAL V1 SENSORY NORMAL?
(X)(N)(Y)	(X)(N)(Y)	TRIGEMINAL V2 SENSORY NORMAL?
(X)(N)(Y)	(X)(N)(Y)	TRIGEMINAL V3 SENSORY NORMAL?
(X)(N)(Y)	(X)(N)(Y)	PALATE REFLEX NORMAL?

(Y)(N) COMMENTS? (V, IX, XI, XII)

(N)(Y) SHOULDER SHRUG NORMAL? . . . . . . IF NO, ABNORMAL . . . . (R)(L)
(N)(Y) TONGUE PROTRUDES TO MIDLINE? IF NO, DEVIATED . . . . (R)(L)
(N)(Y) TONGUE NORMAL, NOT ATROPHIED?
(N)(Y) CLENCH JAW SYMMETRIC? IF NO, DEVIATED . . . . (R)(L)
(N)(Y) PALATE & UVULA MOVEMENT TO MIDLINE? IF NO, DEVIATED . . . . (R)(L)
(N)(Y) GAG REFLEX NORMAL? . . . . IF NO, DEVIATED . . . . (R)(L)

(N)(Y) MENTAL STATUS GROSSLY ORIENTED & NORMAL?
(N)(Y) COMMENTS

IMPRESSION OF ENTIRE NEUROLOGIC EXAM

○ COMPLETELY NORMAL EXAM
○ NORMAL WITH MINOR VARIATIONS NOTED
○ ABNORMAL WITH NO FOLLOW-UP NEEDED
○ ABNORMAL WITH FOLLOW-UP RECOMMENDED

(Y)(N) COMMENTS?

○ LEFT AND RIGHT ACHILLES REFLEX ABSENT?
○ ABNORMAL PINPRICK BOTH FEET?
○ ABNORMAL VIBRATION BOTH ANKLES?

(Y)(N) NERVE CONDUCTION VELOCITY TESTING NEEDED?

NOTE: IF AT LEAST TWO OF THE THREE BUBBLES ARE FILLED IN, AND NERVE CONDUCTION VELOCITY TESTING NEEDED, PROCEED TO NEXT QUESTION.

PRINTED NAME OF PHYSICIAN: **INITIALS/DATE:**

PHYSICIAN'S IMPRESSION OF NERVE CONDUCTION VELOCITY TEST

(Y) YES   (N) NO   HAVE YOU EXPERIENCED SYMPTOMS OF NUMBNESS, TINGLING, BURNING, OR LOSS OF FEELING IN THE FEET?

(R)(L) **NCV TEST CONDUCTED ON WHICH SIDE OF BODY?**
(Y)(N) TEST NORMAL
(Y)(N) COMMENTS?

PRINTED NAME OF EXAMINING PHYSICIAN   **INITIALS/DATE**

FORM QA AUDIT BY:
(1)(2)(3)(4)(5)(6) **INITIALS:**
DATE:

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<table>
<tr><td rowspan="7">PARTICIPANT LABEL</td><td colspan="2" align="center">CASE NUMBER</td><td colspan="2" align="center">GROUP NUMBER</td></tr>
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PARTICIPANT LABEL | **CASE NUMBER** | **GROUP NUMBER**

CASE NUMBER
0 1 2 3 4 5 6 7 8 9
0 1 2 3 4 5 6 7 8 9
0 1 2 3 4 5 6 7 8 9
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0 1 2 3 4 5 6 7 8 9

GROUP NUMBER
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0 1 2 3 4 5 6 7 8 9

EXAMINER I.D.
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0 1 2 3 4 5 6 7 8 9
0 1 2 3 4 5 6 7 8 9
0 1 2 3 4 5 6 7 8 9

UNITED STATES AIR FORCE HEALTH STUDY

YEAR 20 FOLLOW UP

FORM AFHS - 9 ANATOMICAL CHART (SHEET 1 OF 2)

RIGHT

RIGHT   LEFT

Ⓨ Ⓝ **LESION(S) PRESENT ON FRONT**

LESION TYPE LEGEND

1 COMEDONES
2 ACNEIFORM LESIONS
3 ACNEIFORM SCARS
4 DEPIGMENTATION
5 INCLUSION CYSTS
6 CUTIS RHOMBOIDALIS
7 HYPERPIGMENTATION
8 JAUNDICE
9 SPIDER ANGIOMATA
10 PALMAR ERYTHEMA
11 SUSPECTED MELANOMA
12 PALMAR KERATOSES
13 ACTINIC KERATOSES
14 PETECHIAE
15 ECCHYMOSES
16 CONJUNCTIVAL ABNORMALITY

17 ORAL MUCOSAL ABNORMALITY
18 FINGERNAIL ABNORMALITY
19 TOENAIL ABNORMALITY
20 DERMATOGRAPHIA
21 SUS. BASAL CELL CARCINOMA
22 SUS. SQUAMOUS CELL CARCINOMA
23 ATYPICAL/UNUSUAL NEVUS
24 VITILIGO
25 TINEA PEDIS
26 INTERTRIGO
27 LIPOMA
28 ECZEMA
29 PSORIASIS
30 SEBORRHEIC DERMATITIS
31 OTHER ABNORMALITY(IES)

FORM QA AUDIT BY:
① ② ③ ④ ⑤ ⑥ INITIALS:

DATE:

B-18

PARTICIPANT LABEL

CASE NUMBER	GROUP NUMBER
⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨	**EXAMINER I.D.**
⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨

UNITED STATES AIR FORCE HEALTH STUDY

YEAR 20 FOLLOW UP

FORM AFHS - 9 ANATOMICAL CHART (SHEET 2 OF 2)

LEFT

RIGHT

LEFT

Ⓨ Ⓝ **LESION(S) PRESENT ON BACK**

LESION TYPE LEGEND

1	COMEDONES	17	ORAL MUCOSAL ABNORMALITY
2	ACNEIFORM LESIONS	18	FINGERNAIL ABNORMALITY
3	ACNEIFORM SCARS	19	TOENAIL ABNORMALITY
4	DEPIGMENTATION	20	DERMATOGRAPHIA
5	INCLUSION CYSTS	21	SUS. BASAL CELL CARCINOMA
6	CUTIS RHOMBOIDALIS	22	SUS. SQUAMOUS CELL CARCINOMA
7	HYPERPIGMENTATION	23	ATYPICAL/UNUSUAL NEVUS
8	JAUNDICE	24	VITILIGO
9	SPIDER ANGIOMATA	25	TINEA PEDIS
10	PALMAR ERYTHEMA	26	INTERTRIGO
11	SUSPECTED MELANOMA	27	LIPOMA
12	PALMAR KERATOSES	28	ECZEMA
13	ACTINIC KERATOSES	29	PSORIASIS
14	PETECHIAE	30	SEBORRHEIC DERMATITIS
15	ECCHYMOSES	31	OTHER ABNORMALITY(IES)
16	CONJUNCTIVAL ABNORMALITY		

PRINTED NAME OF EXAMINING PHYSICIAN	SIGNATURE/DATE	FORM QA AUDIT BY:
		①②③④⑤⑥ INITIALS:
		DATE:

Mark Reflex® forms by NCS Pearson   MW212102-2   654321   GS99   Printed in U.S.A.

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	**EXAMINER I.D.**
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨

UNITED STATES AIR FORCE HEALTH STUDY

YEAR 20 FOLLOW UP

FORM AFHS - 10 ELECTROCARDIOGRAM REPORT

ECG EXAM WAS/IS:	○ NORMAL ○ NORMAL WITH VARIATIONS	○ ABNORMAL ○ REFUSED
FOLLOW-UP RECOMMENDED?	○ NO	○ YES
PARTICIPANT COMPLY WITH ABSTINENCE?	○ YES	○ NO
TECHNICALLY	○ SATISFACTORY	○ UNSATISFACTORY
RHYTHM: NORMAL SINUS	○ YES	○ NO

RATE

TACHYCARDIA >100
⓪⓪⓪ ①①① ②②② ③③③ ④④④ ⑤⑤⑤ ⑥⑥⑥ ⑦⑦⑦ ⑧⑧⑧ ⑨⑨⑨

BRADYCARDIA <50
⓪⓪ ①① ②② ③③ ④④ ⑤⑤ ⑥⑥ ⑦⑦ ⑧⑧ ⑨⑨

INTERVALS

PR	○ SHORTENED	○ NORMAL	○ PROLONGED
QRS		○ NORMAL	○ PROLONGED
	○ RBBB	○ LBBB	○ OIVCD
QT		○ NORMAL	○ PROLONGED
AXIS:		○ NORMAL	○ RIGHT ○ LEFT

MORPHOLOGY

P-WAVE	○ NORMAL	○ ABNORMAL	
QRS	○ NORMAL	○ ABNORMAL	○ OTHER
ST-T	○ NORMAL	○ ABNORMAL	
Q-WAVE	○ NORMAL	○ ABNORMAL	
U-WAVE	○ PRESENT	○ ABSENT	

CHAMBER ENLARGEMENT

RIGHT ATRIAL	Ⓨ	Ⓝ
LEFT ATRIAL	Ⓨ	Ⓝ
RIGHT VENTRICULAR	Ⓨ	Ⓝ
LEFT VENTRICULAR	Ⓨ	Ⓝ

PRIOR INFARCTION	Ⓨ	Ⓝ
- INFERIOR	○	
- ANTEROSEPTAL	○	
- ANTERIOR	○	
- LATERAL	○	
- POSTERIOR	○	

ARRHYTHMIA? ○ YES
IF YES ➡ NOTE TYPE
- ○ ATRIAL FLUTTER
- ○ ATRIAL FIBRILLATION
- ○ A-V DISSOCIATION
- ○ JUNCTIONAL RHYTHM
- ○ MULTIFOCAL ATRIAL RHYTHM

MULTIFOCAL	UNIFOCAL
○ PVCS	○ PVCS
○ PACS	○ PACS
○ OTHER	

A-V NODAL Ⓨ   Ⓝ

1ST° A-V BLOCK	○
2ND° A-V BLOCK	○
3RD° A-V BLOCK	○

OTHER ○ LOW QRS VOLTAGE
- ○ ANEURYSM   ○ INFERIOR   ○ ANTERIOR   ○ ANTEROSEPTAL   ○ LATERAL
- ○ EARLY REPOLARIZATION
- ○ PRE EXCITATION   ○ WPW   ○ LGL   ○ OTHER

Ⓨ Ⓝ   COMMENTS

TECHNICIANS	ID#	INITIALS
①②③④⑤⑥		

PRINTED NAME OF CARDIOLOGIST/DATE	ID#	INITIALS	FORM QA AUDIT BY: ①②③④⑤⑥ INITIALS:
			DATE:

PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	**EXAMINER I.D.**
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨

FORMS AFHS - 11 RADIOLOGY EXAMINATION - SHEET 1 OF 2

YEAR 20
FOLLOW UP

CHEST X-RAY EXAM WAS:

○ NORMAL, NO FINDINGS
(TYPICAL DEGENERATIVE CHANGES FOR AGE)

○ NORMAL WITH FINDINGS   ○ ABNORMAL   ○ REFUSED

FILM QUALITY IS ACCEPTABLE: Ⓨ YES   Ⓝ NO

FOLLOW-UP NEEDED: Ⓨ YES   Ⓝ NO

COMMENTS/ RECOMMENDATIONS: Ⓨ YES   Ⓝ NO

RIGHT   LEFT

ANTERIOR

(PLEASE NOTE THE LOCATIONS IN ABOVE DIAGRAM)

LUNGS

NORMAL: Ⓨ YES   Ⓝ NO

ABNORMAL:

1. GRANULOMATOUS CHANGES
   - Ⓡ ○ OLD   ○ SUSPECT ACTIVE
   - Ⓛ ○ OLD   ○ SUSPECT ACTIVE

2. INFILTRATE
   - Ⓡ ○ PROBABLY ACUTE   ○ PROBABLY CHRONIC
   - Ⓛ ○ PROBABLY ACUTE   ○ PROBABLY CHRONIC

3. HYPERINFLATION
   - Ⓡ ○ COPD   ○ OTHER
   - Ⓛ ○ COPD   ○ OTHER

4. LESION/NODULE DENSITY
   - Ⓡ ○ PROBABLY BENIGN   ○ POSSIBLY MALIGNANT   ○ CALCIFIED
   - Ⓛ ○ PROBABLY BENIGN   ○ POSSIBLY MALIGNANT   ○ CALCIFIED

5. INTERSTITIAL MARKINGS
   - Ⓡ
   - Ⓛ

6. OTHER
   - Ⓡ _____
   - Ⓛ _____

PRINTED NAME OF X-RAY TECH	ID#	INITIALS/DATE	FORM QA AUDIT BY:
	⓪①②③④⑤⑥⑦⑧		①②③④⑤⑥ INITIALS:
	⓪①②③④⑤⑥⑦⑧		DATE:

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PARTICIPANT LABEL	CASE NUMBER	GROUP NUMBER
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	EXAMINER I.D.
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨
	⓪①②③④⑤⑥⑦⑧⑨	⓪①②③④⑤⑥⑦⑧⑨

UNITED STATES AIR FORCE HEALTH STUDY

YEAR 20 FOLLOW UP

FORMS AFHS - 11 RADIOLOGY EXAMINATION - SHEET 2 OF 2

NORMAL
Ⓨ Ⓝ

SYSTEMIC VASCULATURE

○ DILATED/TORTUOUS AORTA EXCESSIVE FOR AGE
○ ASCENDING ○ DESCENDING ○ ARCH

○ AORTIC ANEURYSM
○ ASCENDING ○ DESCENDING ○ ARCH

○ CALCIFICATIONS EXCESSIVE FOR AGE
○ ASCENDING ○ DESCENDING ○ ARCH

○ OTHER: _____

○ ASCENDING ○ DESCENDING ○ ARCH

Ⓨ Ⓝ

PULMONARY VASCULATURE

○ A/V MALFORMATION   ○ PULMONARY ARTERIAL HYPERTENSION
○ PULMONARY VENOUS CONGESTION ○ OTHER: _____

Ⓨ Ⓝ

DIAPHRAGMS PATHOLOGICALLY ELEVATED Ⓡ Ⓛ ○ HIATAL HERNIA
○ OTHER: _____

Ⓨ Ⓝ

HEART NORMAL

CHAMBER ENLARGEMENT
Ⓡ Ⓛ ATRIAL
Ⓡ Ⓛ VENTRICULAR
Ⓡ Ⓛ OTHER: _____

Ⓨ Ⓝ

PLEURA NORMAL

THICKENED
Ⓡ Ⓛ APICAL
Ⓡ Ⓛ MID
Ⓡ Ⓛ BASE
Ⓡ Ⓛ OTHER: _____

INCIDENTAL FRACTURES (NORMAL): ○ STERNUM ○ SPINE ○ CLAVICLE ○ RIBS

BONY STRUCTURES   NORMAL FOR AGE Ⓨ Ⓝ

RIB ABNORMALITY: ○ CERVICAL
○ HYPOPLASTIC
○ FUSED

DEGENERATIVE CHANGES: ○ CERVICAL
(EXCESSIVE FOR AGE)   ○ DORSAL

SPINAL CURVATURE: ○ SCOLIOSIS
○ KYPHOSIS

COMMENTS Ⓨ Ⓝ _____

POST SURGICAL CHANGES:
○ PRIOR THORACOTOMY (EXCEPT CARDIAC)
○ PRIOR CARDIAC SURGERY (EG., BYPASS, VALVE REPLACEMENT)
○ PACEMAKER/AUTOMATED IMPLANTABLE CARDIAC DEFIBRILLATOR
○ OTHER: _____

PRINTED NAME OF RADIOLOGIST   INITIALS/DATE

PRINTED NAME OF X-RAY TECH	ID#	INITIALS/DATE	FORM QA AUDIT BY:
	⓪①②③④⑤⑥⑦⑧		①②③④⑤⑥ INITIALS:
	⓪①②③④⑤⑥⑦⑧		DATE:

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PARTICIPANT LABEL | **CASE NUMBER** | **GROUP NUMBER**

CASE NUMBER (columns, each with): ⓪①②③④⑤⑥⑦⑧⑨ (repeated 6 rows)

GROUP NUMBER: ⓪①②③④⑤⑥⑦⑧⑨ (2 rows)

EXAMINER I.D.

EXAMINER I.D.: ⓪①②③④⑤⑥⑦⑧⑨ (4 rows)

UNITED STATES AIR FORCE HEALTH STUDY

YEAR 20 FOLLOW UP

FORM AFHS - 14 VASCULAR EXAMINATION - DOPPLER

○ REFUSED

YES NO

Ⓨ Ⓝ   ARE IMAGES ATTACHED? HOW MANY?   ①②③④⑤⑥⑦⑧⑨⑩

Ⓨ Ⓝ   DID PARTICIPANT COMPLY WITH NICOTINE ABSTINENCE REQUIREMENT?

	RIGHT		LEFT	
RADIAL	Ⓧ	⓪①②③	Ⓧ	⓪①②③
FEMORAL	Ⓧ	⓪①②③	Ⓧ	⓪①②③
POPLITEAL	Ⓧ	⓪①②③	Ⓧ	⓪①②③
DORSALIS PEDIS	Ⓧ	⓪①②③	Ⓧ	⓪①②③
POSTERIOR TIBIAL	Ⓧ	⓪①②③	Ⓧ	⓪①②③

X = COULD NOT EXAMINE
0 = NO ARTERIAL FLOW
1 = MONOPHASIC ARTERIAL FLOW
2 = BIPHASIC ARTERIAL FLOW
3 = TRIPHASIC ARTERIAL FLOW

PERIPHERAL SYSTOLIC BLOOD PRESSURE

RESTING ARM PRESSURE — RT / LT (050-350)

Ⓛ Ⓡ ARM WITH MAX PRESSURE

RESTING ANKLE PRESSURE — RT / LT (050-350)

○ NON-COMPRESSIBLE

TOE RAISES 1-120 SECONDS

ANKLE PRESSURE 1 MIN POST EXER — RT / LT (050-350)

ARM PRESSURE 1 MIN POST EXER (050-350)

(Each pressure column with digit bubbles:)
⓪①②③④⑤⑥⑦⑧⑨

ANKLE PRESSURE 2 MIN POST EXER — RT / LT (050-350)

ARM PRESSURE 2 MIN POST EXER (050-350)

FOLLOW UP Ⓨ Ⓝ

COMMENTS/RECOMMENDATIONS: Ⓨ Ⓝ

PRINTED NAME OF TECHNICIAN | **ID#** | **INITIALS/DATE** | **FORM QA AUDIT BY:**

ID#: ⓪①②③④⑤⑥⑦⑧ (2 rows)

FORM QA AUDIT BY: ①②③④⑤⑥ INITIALS:

DATE:

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U.S. AIR FORCE HEALTH STUDY - La Jolla, California

FORM AFHS - 31 EVALUATION

YEAR 20 FOLLOW UP

Dear Health Study Participant:

To serve you and future study participants in the best way possible, please complete this short evaluation form. The form may be completed and delivered to the Health Study Logistics Coordinator following your outbriefing at the Scripps Clinic on the second day of your examination.

	excellent	good	satisfactory	unsatisfactory	not applicable
Initial phone contact and recruitment	○	○	○	○	○
Travel agent contact and travel arrangement	○	○	○	○	○
Logistics Information Packet (mailed)	○	○	○	○	○
Airport/Hotel shuttle service	○	○	○	○	○
Hotel/Clinic van service	○	○	○	○	○
Hotel accommodations	○	○	○	○	○
Evening orientation meeting	○	○	○	○	○
Wives orientation meeting	○	○	○	○	○
Cafeteria meals at the Clinic	○	○	○	○	○
Examination schedule at the Clinic	○	○	○	○	○
Technicians (e.g., blood draw)	○	○	○	○	○
Interviews	○	○	○	○	○
Nursing Staff	○	○	○	○	○
Psychological tests	○	○	○	○	○
Examining physicians	○	○	○	○	○
Clinical outbriefing	○	○	○	○	○
Air Force Health Study Monitor	○	○	○	○	○
Overall clinical experience	○	○	○	○	○

Did any examining physician ask about your specific duties in Southeast Asia? ○ yes ○ no
(If yes, please see the Air Force On-site Monitor immediately)

Ⓨ Ⓝ **Additional comments or acknowledgements:** _____

_____

_____

_____ **Name:** _____
(not required)

Mailing Address:

Air Force Health Study M/S D4
Science Applications International Corporation
10260 Campus Point Drive
San Diego, California 92121

PLEASE DO NOT WRITE IN THIS AREA

◉■■○■■○○■■■○○○○○○○○○○○○○○○○ 1846

FORM AFHS - 33 CHECKLIST FOR PARTICIPANT FOLDER

YEAR 20 FOLLOW UP

CASE NUMBER (columns): ⓪①②③④⑤⑥⑦⑧⑨ (repeated rows)

GROUP NUMBER: ⓪①②③④⑤⑥⑦⑧⑨

EXAMINER I.D.: ⓪①②③④⑤⑥⑦⑧⑨

UNITED STATES AIR FORCE HEALTH STUDY

	EXAM			DATA MGMT			Final QA
	Yes	No	Not App	Yes	No	Not App	

Administrative

Consent Forms

	Yes	No	NA	Yes	No	NA	QA
1. Physical Exam/Psych	Y	N		Y	N		○
2. HIV Testing Informed Consent	Y	N		Y	N		○
3. Future Use of Data	Y	N		Y	N		○
NORC Transmittal Form-Doc to SAIC	Y	N	X	Y	N	X	○
Authorization for Biopsy	Y	N	X	Y	N	X	○
Biopsy Results Follow-up Letter (delayed)	Y	N	X	Y	N	X	○
Copy of Abnormal Letter Encl. (delayed)	Y	N	X	Y	N	X	○
Elevated Glucose Values Follow-up Letter	Y	N	X	Y	N	X	○
Form AFHS-32 List of Physicians	Y	N	X	Y	N	X	○
B&W print of participants digital photo				Y	N	X	○
Blood Perpheral Smear Slide (attached)	Y	N	X	Y	N	X	○
A1:	Y	N	X	Y	N	X	○
A2:	Y	N	X	Y	N	X	○
A3:	Y	N	X	Y	N	X	○
A4:	Y	N	X	Y	N	X	○
A5:	Y	N	X	Y	N	X	○

Medical Forms and Reports

	Yes	No	NA	Yes	No	NA	QA
33 CHECKLIST	Y	N		Y	N		○
16 A MEDICAL SUMMARY	Y	N		Y	N		○
16 B PSYCHOMETRIC SUMMARY	Y	N		Y	N		○
3 A PHYSICAL EXAM PART 1	Y	N		Y	N		○
3 B PHYSICAL EXAM PART 2	Y	N		Y	N		○
4 A DERMATOLOGY	Y	N		Y	N		○
9 ANATOMICAL CHART	Y	N		Y	N		○
4 B DERM - PHYSICAL FEATURES	Y	N	X	Y	N	X	○
5 NEUROLOGY	Y	N		Y	N		○
5 NERVE CONDUCTION VELOCITY	Y	N	X	Y	N	X	○
10 ELECTROCARDIOGRAM REPORT	Y	N		Y	N		○
ECG TRACING	Y	N		Y	N		○
ECG RHYTHM STRIPS	Y	N		Y	N		○
PULMONARY REPORT	Y	N		Y	N		○
11 RADIOLOGY	Y	N	C	Y	N	C	○
14 VASCULAR	Y	N	T	Y	N	T	○
DOPPLER WAVEFORMS	Y	N		Y	N		○
SCL-90-R FORM AND REPORT	Y	N		Y	N		○
WECHSLER WORKSHEET & FORM	Y	N		Y	N		○
LABORATORY REPORT (P) (F)	Y	N		Y	N		○
PATHOLOGY REPORT OF BIOPSY (delayed)	Y	N	X	Y	N	X	○
HISTORY-NORC INTERVIEW RESP	Y	N		Y	N		○
M1:	Y	N	X	Y	N	X	○
M2:	Y	N	X	Y	N	X	○
M3:	Y	N	X	Y	N	X	○
M4:	Y	N	X	Y	N	X	○
M5:	Y	N	X	Y	N	X	○
M6:	Y	N	X	Y	N	X	

INCIDENT: Y N

COMMENT: Y N

NURSE COORDINATOR/DATE | DM RECEIVED BY/DATE

DM QA OFFICER: | FORM QA AUDIT BY: ①②③④⑤⑥⑦ INITIALS: ①②③④⑤⑥⑦ DATE:

LEGEND:
F11: C = CHEST XRAY ENCLOSED
F14: T = TRACINGS ENCLOSED
LAB: F = FINAL OR P = PRELIMINARY RESULTS

PARTICIPANT LABEL | CASE NUMBER | GROUP NUMBER

CASE NUMBER
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨

GROUP NUMBER
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨

EXAMINER I.D.
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨
⓪①②③④⑤⑥⑦⑧⑨

UNITED STATES AIR FORCE HEALTH STUDY

YEAR 20 FOLLOW UP

FORM AFHS - WMS WECHSLER MEMORY SCALE (REVISED)

PARTICIPANT REFUSED ◯

LOGICAL MEMORY - IMMEDIATE

STORY A NUMBER OF MEMORIES
STORY B NUMBER OF MEMORIES

VISUAL REPRODUCTION - IMMEDIATE

PICTURE A   PICTURE B   PICTURE C-1   PICTURE C-2

COMMENT: Ⓨ Ⓝ

(Columns of bubbles ⓪①②③④⑤⑥⑦⑧⑨ for each category)

ASSOCIATE LEARNING

PRESENTATION 1   PRESENTATION 2   PRESENTATION 3
EASY HARD   EASY HARD   EASY HARD

COMMENT: Ⓨ Ⓝ

(Columns of bubbles ⓪①②③④⑤⑥ for each)

LOGICAL MEMORY - DELAYED

STORY A NUMBER OF MEMORIES
STORY B NUMBER OF MEMORIES

VISUAL REPRODUCTION - DELAYED

PICTURE A   PICTURE B   PICTURE C-1   PICTURE C-2

COMMENT: Ⓨ Ⓝ

(Columns of bubbles ⓪①②③④⑤⑥⑦⑧⑨ for each category)

PRINTED NAME OF EXAMINER

ID#
⓪①②③④⑤⑥⑦⑧
⓪①②③④⑤⑥⑦⑧

INITIALS/DATE

FORM QA AUDIT BY:
①②③④⑤⑥ INITIALS:
①②③④⑤⑥
DATE:

▣ SCRIPPS CLINIC

Patient:
Id:
Date:
Technician:

Air Force Health Study

Age: Height(in):   Weight(lb):   Gender:

■ Spirometry

		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Liters						
FEV1	Liters						
FEV1/FVC	%						
FEV3	Liters						
FEV3/FVC	%						
PEF	L/sec						
FEF25-75%	L/sec						
FEF75-85%	L/sec						
FEF50%	L/sec						
FEF75%	L/sec						

Comments:
  Smoking Hx:
  Diagnosis:

Interpretation
  Technical Quality
    adequate   inadequate
  Loss of Vital Capacity
    none   mild   moderate   severe
  Obstructive Abnormality
    none   very mild   mild   moderate   severe
Interpreting Physician.
  Dr. Chang   Dr. Elias   Dr. Soghikian

B-27

SCRIPPS CLINIC MEDICAL LABORATORIES:
10666 N. Torrey Pines Rd., La Jolla, CA 92037   Laboratory Director: E. Lawrence Sakas, M.D.
Air Force Health Study Medical Director, Laboratory Services: Frank W. Hall, M.D.

OUTPATIENT

NAME:
H#   :   LOC: F   AFHS   AGE: SEX:
GRP#:

W53935 COLL: 06/12/2002 07:30 REC: 06/12/2002 08:42 PHYS: Perlman MD (GMED),Monica

ROUTINE CHEMISTRY
    Glucose,Fasting   *160   [70-110]   mg/dL
    Cholesterol   180   [<200]   mg/dL
                             Desirable level <200 mg/dL
                             Low risk 200-240 mg/dL
                             High risl >240 mg/dL

    HDL Cholesterol   *35   [>40]   mg/dL
                             Desirable >40 mg/dL
                             High risk <35 mg/dL

    Triglycerides   73   [<200]   mg/dL
                             Desirable <200 mg/dL
                             High risk >250 mg/dL

    Gamma GT   35   [15-85]   U/L
    Alkaline Phos   86   [50-136]   U/L
    LDH   121   [100-190] U/L
    Creatine Kinase   *30   [35-232]   U/L
    Tot. Bilirubin   0.5   [0.0-1.0] mg/dL
    Dir. Bilirubin   0.2   [0.0-0.3] mg/dL
    Creatinine   1.1   [0.5-1.2] mg/dL
    Amylase   74   [25-115]   U/L
    AST (SGOT)   24   [15-37]   U/L
    ALT (SGPT)   58   [30-65]   U/L
    BUN   22   [7-26]   mg/dL
    Uric Acid   4.4   [3.5-7.2] mg/dL

Diabetes Panel
    Hemoglobin A1c   *7.4   [4.0-6.0] %
    Islet Cell AB   Negative   [NEG]
    GAD Ab.   Negative   [NEG]
    C-Peptide   *7.0   [1.1-5.0] ng/mL
    Proinsulin   *81.4   [2.1-26.8] pmol/L
                    Test Performed by Assoc. Regional & Univ. Pathology Lab,
                     500 Chipeta Way, Salt Lake City, Utah 84108.
                    Laboratory Director Ronald L. Weiss, M.D.

Hepatitis A AB,Total   * POSITIVE   [NEG]

Lupus Panel
    Anti-Nuclear AB   *1:40 Titer   [NEG]
                          Fine speckled
    Anti-Mitochondrial AB
                        Negative   [NEG]
    Anti-Smooth Muscle AB
                        Negative   [NEG]

                              CONTINUED   PAGE 1

AOP-12L

NOTE: FINAL CHART COPY: NOT TO BE REMOVED.

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SCRIPPS CLINIC MEDICAL LABORATORIES:
10666 N. Torrey Pines Rd., La Jolla, CA 92037   Laboratory Director: E. Lawrence Sakas, M.D.
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OUTPATIENT

NAME:
H# :   LOC: F   AFHS   AGE: SEX:
GRP#:

W53935   COLL: 06/12/2002 07:30 REC: 06/12/2002 08:42 PHYS: Perlman MD (GMED),Monica

Lupus Panel   (CONTINUED)
  Anti-Parietal Cell AB
                         Negative   [NEG]
  Thyroid Microsomal AB
                         Negative   [NEG]
  Rheumatoid Factor   *129   [<20]   IU/mL

OCCULT BLOOD PANEL
  Occult Blood 1   NONREACTIVE   [NR]
  Occult Blood 2   NONREACTIVE   [NR]
  Occult Blood 3   [NR]
                    * Specimen not applied

Miscellaneous Chemistry
  FSH   6.9   [1.4-18.1] mIU/mL
  LH   4.4   [2-12]   mIU/mL
  TSH   2.52   [0.35-5.50] uIU/mL
  Testosterone,Free   10.6   [6-20]   pg/mL
  Estradiol   <10   [<53]   pg/mL
  Testosterone, Total   475   [241-827] ng/dL
  T4,Free   1.11   [0.89-1.76] ng/dL
  PSA   *4.1   [0.0-4.0] ng/mL
  Insulin,Fasting   17   [6-27]   uIU/mL

Anti-Thyroid ABS   Negative   [NEG]

Quant. Fibrinogen   *600   [170-450] mg/dL

Prothromin Time   11.3   [9.2-12.3] sec.

CELL COUNT/INDICES
  WBC   7.8   [4.5-11.0] K/cumm
  RBC   4.38   [4.30-5.90] M/cumm
  HGB   *13.6   [13.9-18.0] g/dL
  HCT   42.1   [39.0-55.0] %
  MCV   96.3   [80.0-97.0] cu.micr
  MCH   31.2   [26.0-34.0] pg
  MCHC   32.4   [31.0-37.0] g/dL
  PLT   236   [130-400] K/cumm

DIFFERENTIAL
  Segs   56   [45-66]   %
  Bands   5   [0-10]   %
  Lymphs   25   [15-41]   %
  Monos   10   [4-12]   %
  Eos   1   [0-5]   %
  Basos   2   [0-2]   %

                          CONTINUED

FINAL REPORT

PAGE 2

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SCRIPPS CLINIC MEDICAL LABORATORIES:
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OUTPATIENT

NAME:
H#   :   LOC: F   AFHS   AGE: SEX:
GRP#:

W53935 COLL: 06/12/2002 07:30 REC: 06/12/2002 08:42 PHYS: Perlman MD (GMED),Monica

DIFFERENTIAL   (CONTINUED)
```
  RBC Morphology       * Sl Aniso        [NORM]
  PLT Observation        Adequate        [ADEQ]
  WBC Morphology         None
  Metas                *1                [0]           %
  ABS Segs              4.36             [1.5-8.5]  K/cumm
  ABS Bands             0.39             [0.0-1.0]  K/cumm
  ABS Lymphs            1.95             [1.0-4.8]  K/cumm
  ABS Monos             0.78             [0.2-0.8]  K/cumm
  ABS Eos              0.08             [0.0-0.7]  K/cumm
  ABS Basos            0.16             [0.0-0.2]  K/cumm
  ABS Metas           *0.08             [0]        K/cumm

SED RATE             *54               [0-20]     mm/hr

URINALYSIS
  Color                Yellow            [YELLOW]
  Clarity              Clear             [CLEAR]
  Spec. grav.          1.030             [1.005-1.030]
  pH                   5.5               [5.0-8.5]
  Protein              Negative          [NEG]      mg/dL
  Glucose             *>=1.00            [NEG]      g/dL
  Ketones              Negative          [NEG]      mg/dL
  Bilirubin            Negative          [NEG]
  Blood                Negative          [NEG]
  Nitrites             Negative          [NEG]
  Urobilinogen         1.0               [<2.0]     mg/dL
  Leuk Esterase        Negative          [NEG]
  Casts                None              [NONE]     /LPF
  Crystals             None              [NONE]     /HPF
  Wbc                  0-2               [ZT2]      /HPF
  Rbc                  0-2               [ZT2]      /HPF
  Epithelial cells    * Few              [NONE]     /HPF
                        Squamous
  Bacteria            * Few              [NONE]     /HPF
  Mucus               * Few              [NONE]     /HPF
  Other                None              [NONE]
  Comment              None

PROTEIN PROFILE
  Prealbumin           22.3              [18.0-38.0] mg/dL
  Albumin              3.9               [3.4-5.0] g/dL
  a-1-Acid Glycoprotein
                       107               [51-117]   mg/dL
  a-1-Antitrypsin     *184               [88-174]   mg/dL
  a-2-Macroglobulin   *393               [102-259] mg/dL
  Apolipoprotein B     107               [56-162]   mg/dL
```

CONTINUED   PAGE 3

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W53935 COLL: 06/12/2002 07:30 REC: 06/12/2002 08:42 PHYS: Perlman MD (GMED),Monica

PROTEIN PROFILE   (CONTINUED)
    C3 Complement   128   [79-152] mg/dL
    C4 Complement   19   [16-38]   mg/dL
    Haptoglobin   *220   [36-195] mg/dL
    IgA   *597   [82-453] mg/dL
    IgG   1180   [751-1560] mg/dL
    IgM   111   [46-304] mg/dL
    Transferrin   206   [202-336] mg/dL

AF LYMPHOCYTE PHENOTYPING PANEL
    WBC count   7.8   [4.5-11.0] K/cumm
    % Lymphs   25   [24-44]   %
    Abs. Lymphs   1950   [1100-4800] /cumm
    CD45 Total lymphs(CD14-)
                         94   %
    CD3 T cells   59   [56-90]   %
    Abs. CD3   1151   [700-2400] /cumm
    CD4   43   [30-60]   %
    Abs. CD4   839   [400-1400] /cumm
    CD4+CD3   38   [30-60]   %
    AB. CD4+CD3   741   [400-1400] /cumm
    CD8   37   [18-40]   %
    Abs. CD8   722   [300-900] /cumm
    CD8+CD3   19   [18-40]   %
    AB. CD8+CD3   371   [300-900] /cumm
    CD16/56 NK cells   *27   [2-25]   %
    Abs. CD16/56   527   /cumm
    CD20 B Cells   10   [3-18]   %
    Abs. CD20   195   /cumm

DAY 1   FASTING

W53936 COLL: 06/12/2002 07:30 REC: 06/12/2002 08:42 PHYS: Perlman MD (GMED),Monica

Microalbumin
    Microalbumin Screen * POSITIVE   [NEG]
    Urine Creatinine   80   [30-125] mg/dL
    Microalbumin (Quant) 1.4   [<1.9]   mg/dL
    Ratio   17.50   [<30.0]   ug/mg

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END OF REPORT   PAGE 4

AOP-12L

NOTE: FINAL CHART COPY. NOT TO BE REMOVED.

SCL-90-R®
Symptom Checklist-90-R
Leonard R. Derogatis, PhD

MICROTEST Q™
Assessment System

NAME (Optional)

DIRECTIONS:

1. When you record your responses on this answer sheet, use a No. 2 pencil only, and fill in the circles with a heavy, dark mark.

2. Print your identification number in the box to the left. Then find the circle below each space that has the same number and blacken it. In a similar way, complete the Birth Date and Test Date boxes.

3. Blacken the appropriate circle for your gender.

4. If you want to change a response, erase it carefully and then fill in your new choice.

5. Do not make any marks outside the circles.

IDENTIFICATION NUMBER

0	0	0	0	0	0	0	0	0	0
1	1	1	1	1	1	1	1	1	1
2	2	2	2	2	2	2	2	2	2
3	3	3	3	3	3	3	3	3	3
4	4	4	4	4	4	4	4	4	4
5	5	5	5	5	5	5	5	5	5
6	6	6	6	6	6	6	6	6	6
7	7	7	7	7	7	7	7	7	7
8	8	8	8	8	8	8	8	8	8
9	9	9	9	9	9	9	9	9	9

BIRTH DATE

MONTH | DAY | YEAR

TEST DATE

MONTH | DAY | YEAR

GENDER
1. Male
2. Female

PLEASE DO NOT MARK IN THIS AREA

156162

Product Number
51417

B-32

INSTRUCTIONS:

Below is a list of problems people sometimes have. Please read each one carefully, and blacken the circle that best describes HOW MUCH THAT PROBLEM HAS DISTRESSED OR BOTHERED YOU DURING THE PAST 7 DAYS INCLUDING TODAY. Blacken the circle for only one number for each problem and do not skip any items. If you change your mind, erase your first mark carefully. Read the example before beginning, and if you have any questions please ask them now.

EXAMPLE

	NOT AT ALL	A LITTLE BIT	MODERATELY	QUITE A BIT	EXTREMELY	HOW MUCH WERE YOU DISTRESSED BY:
1	⓪	①	②	●	④	Bodyaches

HOW MUCH WERE YOU DISTRESSED BY:

	NOT AT ALL	A LITTLE BIT	MODERATELY	QUITE A BIT	EXTREMELY	
1	⓪	①	②	③	④	Headaches
2	⓪	①	②	③	④	Nervousness or shakiness inside
3	⓪	①	②	③	④	Repeated unpleasant thoughts that won't leave your mind
4	⓪	①	②	③	④	Faintness or dizziness
5	⓪	①	②	③	④	Loss of sexual interest or pleasure
6	⓪	①	②	③	④	Feeling critical of others
7	⓪	①	②	③	④	The idea that someone else can control your thoughts
8	⓪	①	②	③	④	Feeling others are to blame for most of your troubles
9	⓪	①	②	③	④	Trouble remembering things
10	⓪	①	②	③	④	Worried about sloppiness or carelessness
11	⓪	①	②	③	④	Feeling easily annoyed or irritated
12	⓪	①	②	③	④	Pains in heart or chest
13	⓪	①	②	③	④	Feeling afraid in open spaces or on the streets
14	⓪	①	②	③	④	Feeling low in energy or slowed down
15	⓪	①	②	③	④	Thoughts of ending your life
16	⓪	①	②	③	④	Hearing voices that other people do not hear
17	⓪	①	②	③	④	Trembling
18	⓪	①	②	③	④	Feeling that most people cannot be trusted
19	⓪	①	②	③	④	Poor appetite
20	⓪	①	②	③	④	Crying easily
21	⓪	①	②	③	④	Feeling shy or uneasy with the opposite sex
22	⓪	①	②	③	④	Feelings of being trapped or caught
23	⓪	①	②	③	④	Suddenly scared for no reason
24	⓪	①	②	③	④	Temper outbursts that you could not control
25	⓪	①	②	③	④	Feeling afraid to go out of your house alone
26	⓪	①	②	③	④	Blaming yourself for things
27	⓪	①	②	③	④	Pains in lower back
28	⓪	①	②	③	④	Feeling blocked in getting things done
29	⓪	①	②	③	④	Feeling lonely
30	⓪	①	②	③	④	Feeling blue
31	⓪	①	②	③	④	Worrying too much about things
32	⓪	①	②	③	④	Feeling no interest in things
33	⓪	①	②	③	④	Feeling fearful
34	⓪	①	②	③	④	Your feelings being easily hurt
35	⓪	①	②	③	④	Other people being aware of your private thoughts
36	⓪	①	②	③	④	Feeling others do not understand you or are unsympathetic
37	⓪	①	②	③	④	Feeling that people are unfriendly or dislike you

	NOT AT ALL	A LITTLE BIT	MODERATELY	QUITE A BIT	EXTREMELY	HOW MUCH WERE YOU DISTRESSED BY:
38	0	1	2	3	4	Having to do things very slowly to insure correctness
39	0	1	2	3	4	Heart pounding or racing
40	0	1	2	3	4	Nausea or upset stomach
41	0	1	2	3	4	Feeling inferior to others
42	0	1	2	3	4	Soreness of your muscles
43	0	1	2	3	4	Feeling that you are watched or talked about by others
44	0	1	2	3	4	Trouble falling asleep
45	0	1	2	3	4	Having to check and double-check what you do
46	0	1	2	3	4	Difficulty making decisions
47	0	1	2	3	4	Feeling afraid to travel on buses, subways, or trains
48	0	1	2	3	4	Trouble getting your breath
49	0	1	2	3	4	Hot or cold spells
50	0	1	2	3	4	Having to avoid certain things, places, or activities because they frighten you
51	0	1	2	3	4	Your mind going blank
52	0	1	2	3	4	Numbness or tingling in parts of your body
53	0	1	2	3	4	A lump in your throat
54	0	1	2	3	4	Feeling hopeless about the future
55	0	1	2	3	4	Trouble concentrating
56	0	1	2	3	4	Feeling weak in parts of your body
57	0	1	2	3	4	Feeling tense or keyed up
58	0	1	2	3	4	Heavy feelings in your arms or legs
59	0	1	2	3	4	Thoughts of death or dying
60	0	1	2	3	4	Overeating
61	0	1	2	3	4	Feeling uneasy when people are watching or talking about you
62	0	1	2	3	4	Having thoughts that are not your own
63	0	1	2	3	4	Having urges to beat, injure, or harm someone
64	0	1	2	3	4	Awakening in the early morning
65	0	1	2	3	4	Having to repeat the same actions such as touching, counting, or washing
66	0	1	2	3	4	Sleep that is restless or disturbed
67	0	1	2	3	4	Having urges to break or smash things
68	0	1	2	3	4	Having ideas or beliefs that others do not share
69	0	1	2	3	4	Feeling very self-conscious with others
70	0	1	2	3	4	Feeling uneasy in crowds, such as shopping or at a movie
71	0	1	2	3	4	Feeling everything is an effort
72	0	1	2	3	4	Spells of terror or panic
73	0	1	2	3	4	Feeling uncomfortable about eating or drinking in public
74	0	1	2	3	4	Getting into frequent arguments
75	0	1	2	3	4	Feeling nervous when you are left alone
76	0	1	2	3	4	Others not giving you proper credit for your achievements
77	0	1	2	3	4	Feeling lonely even when you are with people
78	0	1	2	3	4	Feeling so restless you couldn't sit still
79	0	1	2	3	4	Feelings of worthlessness
80	0	1	2	3	4	The feeling that something bad is going to happen to you
81	0	1	2	3	4	Shouting or throwing things
82	0	1	2	3	4	Feeling afraid you will faint in public
83	0	1	2	3	4	Feeling that people will take advantage of you if you let them
84	0	1	2	3	4	Having thoughts about sex that bother you a lot
85	0	1	2	3	4	The idea that you should be punished for your sins
86	0	1	2	3	4	Thoughts and images of a frightening nature
87	0	1	2	3	4	The idea that something serious is wrong with your body
88	0	1	2	3	4	Never feeling close to another person
89	0	1	2	3	4	Feelings of guilt
90	0	1	2	3	4	The idea that something is wrong with your mind

| MNC RECORD | # 2 | Median Motor.R | 14:40:03 |

Switch: STOP Stim: 1 | Rate: 1.0 Hz | Level: 163 V | Dur: 0.1 ms | Single

| Step: Hold | Average: Off | Rectify: Off |
| Trace Delay: 0 ms | |
| Birth Date: 16 NOV 30 00 Male |
| Exam. Date: 1 JAN 78 00 Age: 47Y 46D |

2 ms

A 1   235V
       5 mV

Recording Site : APB

STIMULUS SITE	LAT1 ms	LAT2 ms	AMP mV	TEMP °C
A1: Wrist	4.3	10.4	8.530	32.8
A2: Elbow	8.9	15.3	7.801	32.7

A 2   400V
       5 mV

SEGMENT	DIST mm	DIFF ms	CV m/s	TEMP °C
Wrist-Elbow	250	4.6	54	32.7

TEMP: 32.4°C

F-WAVES RECORD   # 2   Median Nerve.R   14:39:40
                                                      .R

| Switch: N-R Stim: 1 | Rate:Non-Recurrent | Level: | 163 V | Dur: 0.1 ms | Single |

| Trace: | 15/16 | | |
| Distance: |

Stim:

Birth Date: 16 NOV 30 00   Male
Exam. Date: 6 JUN 78 00   Age: 47Y 202D

| M-LAT: 4.4 ms | M-Amp: 13.78 mV |

| TEMP: 32.4 °C | F-LAT: 29.1 ms |

5 mV   F-SNS: 500 uV   5 ms

163V
163V
163V
163V
163V
163V
163V
163V
163V
163V
163V
163V
163V
163V

5 mV   F-SNS: 500 uV   5 ms

| SNC RECORD | # 2 | Median Sensory.R | 14:29:39 |

| Switch: STOP / Stim: 1 | Rate: 1.0 Hz | Level: 97.3 mA | Dur: 0.1 ms | Single |

| Step: 1 | Average: ▮ | Rectify: Off |
| Trace Delay: | 0 ms | |

Birth Date: 16 NOV 30 00   Male
Exam. Date: 1 JAN 78 00   Age: 47Y 46D

Recording Site :wrist

```
1 ms
                                             97.3mA
A                                            10 uV
1                                            N:   9
```

STIMULUS SITE	LAT1 ms	LAT2 ms	AMP uV	TEMP °C
A1: index	3.1	3.6	3.723	34.1

SEGMENT	DIST mm	CV m/s	TEMP °C
wrist-index	140	45	34.1

TEMP: 33.0°C

| SNC RECORD | # 3 | Ulnar Sensory.R | 14:36:10 |

| Switch: STOP Stim: 1 | Rate: | 0.5 Hz | Level: 76.1 mA | Dur: 0.1 ms | Single |

Step: 1	Average:	Rectify: Off
Trace Delay:	0 ms	
Birth Date:	16 NOV 30 00	Male
Exam. Date:	1 JAN 78 00	Age: 47Y 46D

1 ms

76.1mA
10 uV
N: 3

A
1

Recording Site :wrist

STIMULUS SITE	LAT1 ms	LAT2 ms	AMP uV	TEMP °C
A1: index	3.0	3.6	2.684	32.5

SEGMENT	DIST mm	DIFF ms	CV m/s	TEMP °C
wrist-index	140	3.0	46	32.5

TEMP: 32.5°C

| MNC RECORD | # 1 | tibial motor.R | 14:19:17 |

| Switch: STOP Stim: 1 | Rate: | 1.0 Hz | Level: | 400 V | Dur: 0.5 ms | Single |

| Step: Hold | Average: Off | Rectify: Off |
| Trace Delay: | 0 ms | |
| Birth Date: 16 NOV 30 00   Male |
| Exam. Date: 1 JAN 78 00   Age: 47Y 460 |

5 ms

400V
1 mV

A
1

400V
1 mV

A
2

TEMP: 32.4°C

Recording Site : abductor hallucis

STIMULUS SITE	LAT1 ms	AMP mV	TEMP °C
A1: ankle	4.1	3.621	32.9
A2: pop. fossa	14.9	1.699	33.1

SEGMENT	DIST mm	DIFF ms	CV m/s	TEMP °C
ankle-pop. fossa	426	10.8	39	33.1

F-WAVES RECORD   # 1   tibial.R   14:20:10
                                                     .R

| Switch: STOP | Rate: | 0.7 Hz | Level: | 400 V | Dur: 0.2 ms | Single |
| Stim: 1 | | | | | | |

| 5 mV | F-SNS: 500 uV | 10 ms |

Trace: 12/16
                                    Distance:
Stim:
Birth Date: 16 NOV 30 00   Male
Exam. Date: 6 JUN 78 00   Age: 47Y 202D

| M-LAT: 5.3 ms | M-Amp: 3.034 mV |

| TEMP: 32.3 °C | F-LAT: 60.8 ms |

400V
400V
400V
400V
400V
400V
400V
400V
400V
400V
400V

| 5 mV | F-SNS: 500 uV | 10 ms |

| SNC RECORD | # 1 | Sural Sensory.R | 14:24:45 |

| Switch: STOP / Stim: 1 | Rate: | 0.5 Hz | Level: 80.0 mA | Dur: 0.1 ms | Single |

Step: 1		Average: ▇	Rectify: Off
Trace Delay:	0 ms		
Birth Date: 16 NOV 30 00	Male		
Exam. Date: 1 JAN 78 00	Age: 47Y 46D		

1 ms

Stimulus Site : Ankle

RECORDING SITE	LAT1 ms	LAT2 ms	AMP uV	TEMP °C
A1: Sur 1	3.1	3.8	3.452	33.2

A 1

80.0mA
10 uV
N: 7

SEGMENT	DIST mm	CV m/s	TEMP °C
Ankle-Sur 1	140	45	33.2

TEMP: 33.3°C

APPENDIX **C**

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Table C-1. Compliance of Ranch Hands by Examination Year

Time Period	Disposition	Compliance at the Baseline Examination					
		FC	PC	R	UNL	NS	Total
Baseline Examination		*1,046*	*127*	*34*	*2*	*--*	*1,209*
1985 Examination	**Eligible**	*1,046*	*127*	*34*	*2*	*--*	*1,209*
Between Baseline and	New to Study	--	--	--	--	9	9
1985 Examinations	Deceased	(10)	(9)	(0)	(0)	(0)	(19)
	Remaining Eligible	*1,036*	*118*	*34*	*2*	*9*	*1,199*
	Unlocatable	(27)	(12)	(0)	(0)	(0)	(39)
	Refused	(37)	(66)	(29)	(1)	(0)	(133)
	Partially Compliant	(0)	(1)	(5)	(0)	(4)	(10)
	Fully Compliant	*972*	*39*	*0*	*1*	*5*	*1,017*
1987 Examination	**Eligible**	*1,036*	*118*	*34*	*2*	*9*	*1,199*
Between 1985 and	New to Study	--	--	--	--	4	4
1987 Examinations	Deceased	(12)	(2)	(1)	(0)	(0)	(15)
	Remaining Eligible	*1,024*	*116*	*33*	*2*	*13*	*1,188*
	Unlocatable	(8)	(10)	(2)	(0)	(0)	(20)
	Refused	(71)	(69)	(27)	(1)	(3)	(171)
	Partially Compliant	--	--	(1)	(0)	(0)	(1)
	Fully Compliant	*945*	*37*	*3*	*1*	*10*	*996*
1992 Examination	**Eligible**	*1,024*	*116*	*33*	*2*	*13*	*1,188*
Between 1987 and	New to Study	--	--	--	--	0	(0)
1992 Examinations	Deceased	(35)	(2)	(2)	(0)	(0)	(39)
	Remaining Eligible	*989*	*114*	*31*	*2*	*13*	*1,149*
	Unlocatable	(5)	(4)	(2)	(1)	(0)	(12)
	Refused	(82)	(75)	(23)	(0)	(4)	(184)
	Fully Compliant	*902*	*35*	*6*	*1*	*9*	*953*
1997 Examination	**Eligible**	*989*	*114*	*31*	*2*	*13*	*1,149*
Between 1992 and	New to Study	--	--	--	--	0	(0)
1997 Examinations	Deceased	(39)	(7)	(1)	(0)	(0)	(47)
	Remaining Eligible	*950*	*107*	*30*	*2*	*13*	*1,102*
	Unlocatable	(1)	(0)	(2)	(1)	(0)	(4)
	Refused	(129)	(71)	(23)	(0)	(4)	(227)
	Not Contacted	(1)	(0)	(0)	(0)	(0)	(1)
	Fully Compliant	*819*	*36*	*5*	*1*	*9*	*870*
2002 Examination	**Eligible**	*950*	*107*	*30*	*2*	*13*	*1,102*
Between 1997 and	New to Study	--	--	--	--	1	1
2002 Examinations	Deceased	(54)	(3)	(1)	(0)	(0)	(58)
	Discovered to be Ineligible	(1)	(0)	(0)	(0)	(1)	(2)
	Remaining Eligible	*895*	*104*	*29*	*2*	*13*	*1,043*
	Unlocatable	(2)	(0)	(0)	(1)	(0)	(3)
	Refused	(166)	(68)	(24)	(0)	(4)	(262)
	Not Contacted	(1)	(0)	(0)	(0)	(0)	(1)
	Fully Compliant	*726*	*36*	*5*	*1*	*9*	*777*

FC = Fully Compliant at Baseline Examination   UNL = Unlocatable at Baseline Examination
PC = Partially Compliant at Baseline Examination   NS = New to Study Since Baseline Examination
R = Refusal at Baseline Examination   -- = Undefined Categories

Table C-2. Compliance of All Comparisons by Examination Year

Time Period	Disposition	Compliance at the Baseline Examination					
		FC	PC	R	UNL	NS	Total
Baseline Examination		*1,223*	*301*	*133*	*9*	*--*	*1,666*
1985 Examination	*Eligible*	*1,223*	*301*	*133*	*9*	*--*	*1,666*
Between Baseline and	New to Study	--	--	--	--	73	73
1985 Examinations	Deceased	(16)	(9)	(1)	(0)	(0)	(26)
	Remaining Eligible	*1,207*	*292*	*132*	*9*	*73*	*1,713*
	Unlocatable	(38)	(26)	(0)	(0)	(1)	(65)
	Refused	(31)	(172)	(87)	(5)	(30)	(325)
	Partially Compliant	(0)	(1)	(24)	(0)	(6)	(31)
	Fully Compliant	*1,138*	*93*	*21*	*4*	*36*	*1,292*
1987 Examination	*Eligible*	*1,207*	*292*	*132*	*9*	*73*	*1,713*
Between 1985 and	New to Study	--	--	--	--	33	33
1987 Examinations	Deceased	(14)	(1)	(1)	(0)	(0)	(16)
	Remaining Eligible	*1,193*	*291*	*131*	*9*	*106*	*1,730*
	Unlocatable	(8)	(20)	(9)	(3)	(7)	(47)
	Refused	(73)	(178)	(88)	(3)	(16)	(358)
	Partially Compliant	--	--	(13)	(0)	(14)	(27)
	Fully Compliant	*1,112*	*93*	*21*	*3*	*69*	*1,298*
1992 Examination	*Eligible*	*1,193*	*291*	*131*	*9*	*106*	*1,730*
Between 1987 and	New to Study	--	--	--	--	83	83
1992 Examinations	Deceased	(37)	(8)	(1)	(0)	(6)	(52)
	Remaining Eligible	*1,156*	*283*	*130*	*9*	*183*	*1,761*
	Unlocatable	(9)	(8)	(7)	(3)	(29)	(56)
	No Health-Match	--	--	--	--	(11)	(11)
	Refused	(85)	(179)	(95)	(3)	(52)	(414)
	Fully Compliant	*1,062*	*96*	*28*	*3*	*91*	*1,280*
1997 Examination	*Eligible*	*1,156*	*283*	*130*	*9*	*183*	*1,761*
Between 1992 and	New to Study	--	--	--	--	236	236
1997 Examinations	No Health-Match in 1992	--	--	--	--	(11)	(11)
	Deceased	(40)	(9)	(2)	(0)	(15)	(66)
	Remaining Eligible	*1,116*	*274*	*128*	*9*	*393*	*1,920*
	Unlocatable	(4)	(4)	(7)	(2)	(13)	(30)
	No Health-Match	--	--	--	--	(91)	(91)
	Refused	(136)	(176)	(91)	(3)	(142)	(548)
	Fully Compliant	*976*	*94*	*30*	*4*	*147*	*1,251*
2002 Examination	*Eligible*	*1,116*	*274*	*128*	*9*	*393*	*1,920*
Between 1997 and	New to Study	--	--	--	--	318	318
2002 Examinations	No Health-Match in 1997	--	--	--	--	(91)	(91)
	Deceased	(59)	(11)	(4)	(1)	(25)	(100)
	Discovered to be Ineligible	(1)	(0)	(0)	(0)	(2)	(3)
	Remaining Eligible	*1,056*	*263*	*124*	*8*	*593*	*2,044*
	Unlocatable	(4)	(4)	(2)	(2)	(20)	(32)
	No Health-Match	--	--	--	--	(60)	(60)
	Refused	(188)	(177)	(97)	(5)	(311)	(778)
	Fully Compliant	*864*	*82*	*25*	*1*	*202*	*1,174*

FC = Fully Compliant at Baseline Examination   UNL = Unlocatable at Baseline Examination
PC = Partially Compliant at Baseline Examination   NS = New to Study Since Baseline Examination
R = Refusal at Baseline Examination   -- = Undefined Categories

Table C-3. Compliance of Original Comparisons by Examination Year

Time Period	Disposition	Compliance at the Baseline Examination					
		FC	PC	R	UNL	NS	Total
Baseline Examination		*935*	*216*	*81*	*3*	*--*	*1,235*
1985 Examination	*Eligible*	*935*	*216*	*81*	*3*	*--*	*1,235*
Between Baseline and	New to Study	--	--	--	--	17	17
1985 Examinations	Deceased	(11)	(9)	(1)	(0)	(0)	(21)
	Remaining Eligible	*924*	*207*	*80*	*3*	*17*	*1,231*
	Unlocatable	(28)	(19)	(0)	(0)	(1)	(48)
	Refused	(25)	(126)	(62)	(2)	(4)	(219)
	Partially Compliant	(0)	(1)	(8)	(0)	(1)	(10)
	Fully Compliant	*871*	*61*	*10*	*1*	*11*	*954*
1987 Examination	*Eligible*	*924*	*207*	*80*	*3*	*17*	*1,231*
Between 1985 and	New to Study	--	--	--	--	4	4
1987 Examinations	Deceased	(12)	(1)	(0)	(0)	(0)	(13)
	Remaining Eligible	*912*	*206*	*80*	*3*	*21*	*1,222*
	Unlocatable	(7)	(12)	(9)	(2)	(1)	(31)
	Refused	(51)	(131)	(53)	(1)	(6)	(242)
	Partially Compliant	--	--	(11)	(0)	(0)	(11)
	Fully Compliant	*854*	*63*	*7*	*0*	*14*	*938*
1992 Examination	*Eligible*	*912*	*206*	*80*	*3*	*21*	*1,222*
Between 1987 and	New to Study	--	--	--	--	2	2
1992 Examinations	Deceased	(25)	(6)	(0)	(0)	(2)	(33)
	Remaining Eligible	*887*	*200*	*80*	*3*	*21*	*1,191*
	Unlocatable	(6)	(4)	(3)	(2)	(0)	(15)
	Refused	(61)	(132)	(64)	(1)	(6)	(264)
	Fully Compliant	*820*	*64*	*13*	*0*	*15*	*912*
1997 Examination	*Eligible*	*887*	*200*	*80*	*3*	*21*	*1,191*
Between 1992 and	New to Study	--	--	--	--	2	2
1997 Examinations	Deceased	(32)	(9)	(1)	(0)	(0)	(42)
	Remaining Eligible	*855*	*191*	*79*	*3*	*23*	*1,151*
	Unlocatable	(3)	(3)	(4)	(0)	(0)	(10)
	Refused	(106)	(125)	(61)	(2)	(8)	(302)
	Fully Compliant	*746*	*63*	*14*	*1*	*15*	*839*
2002 Examination	*Eligible*	*855*	*191*	*79*	*3*	*23*	*1,151*
Between 1997 and	New to Study	--	--	--	--	1	1
2002 Examinations	Deceased	(49)	(7)	(1)	(0)	(0)	(57)
	Discovered to be Ineligible	(1)	(0)	(0)	(0)	(1)	(2)
	Remaining Eligible	*805*	*184*	*78*	*3*	*23*	*1,093*
	Unlocatable	(3)	(3)	(1)	(0)	(0)	(7)
	Refused	(147)	(126)	(65)	(3)	(8)	(349)
	Fully Compliant	*655*	*55*	*12*	*0*	*15*	*737*

FC = Fully Compliant at Baseline Examination   UNL = Unlocatable at Baseline Examination
PC = Partially Compliant at Baseline Examination   NS = New to Study Since Baseline Examination
R = Refusal at Baseline Examination   -- = Undefined Categories

Table C-4. Compliance of Replacement Comparisons by Examination Year

Time Period	Disposition	Compliance at the Baseline Examination					
		FC	PC	R	UNL	NS	Total
Baseline Examination		*288*	*85*	*52*	*6*	*--*	*431*
1985 Examination	*Eligible*	*288*	*85*	*52*	*6*	*--*	*431*
Between Baseline and	New to Study	--	--	--	--	56	56
1985 Examinations	Deceased	(5)	(0)	(0)	(0)	(0)	(5)
	Remaining Eligible	*283*	*85*	*52*	*6*	*56*	*482*
	Unlocatable	(10)	(7)	(0)	(0)	(0)	(17)
	Refused	(6)	(46)	(25)	(3)	(26)	(106)
	Partially Compliant	(0)	(0)	(16)	(0)	(5)	(21)
	Fully Compliant	*267*	*32*	*11*	*3*	*25*	*338*
1987 Examination	*Eligible*	*283*	*85*	*52*	*6*	*56*	*482*
Between 1985 and	New to Study	--	--	--	--	29	29
1987 Examinations	Deceased	(2)	(0)	(1)	(0)	(0)	(3)
	Remaining Eligible	*281*	*85*	*51*	*6*	*85*	*508*
	Unlocatable	(1)	(8)	(0)	(1)	(6)	(16)
	Refused	(22)	(47)	(35)	(2)	(10)	(116)
	Partially Compliant	(0)	(0)	(2)	(0)	(14)	(16)
	Fully Compliant	*258*	*30*	*14*	*3*	*55*	*360*
1992 Examination	*Eligible*	*281*	*85*	*51*	*6*	*85*	*508*
Between 1987 and	New to Study	--	--	--	--	81	81
1992 Examinations	Deceased	(12)	(2)	(1)	(0)	(4)	(19)
	Remaining Eligible	*269*	*83*	*50*	*6*	*162*	*570*
	Unlocatable	(3)	(4)	(4)	(1)	(29)	(41)
	No Health-Match	--	--	--	--	(11)	(11)
	Refused	(24)	(47)	(31)	(2)	(46)	(150)
	Fully Compliant	*242*	*32*	*15*	*3*	*76*	*368*
1997 Examination	*Eligible*	*269*	*83*	*50*	*6*	*162*	*570*
Between 1992 and	New to Study	--	--	--	--	234	234
1997 Examinations	No Health-Match in 1992	--	--	--	--	(11)	(11)
	Deceased	(8)	(0)	(1)	(0)	(15)	(24)
	Remaining Eligible	*261*	*83*	*49*	*6*	*370*	*769*
	Unlocatable	(1)	(1)	(3)	(2)	(13)	(20)
	No Health-Match	--	--	--	--	(91)	(91)
	Refused	(30)	(51)	(30)	(1)	(134)	(246)
	Fully Compliant	*230*	*31*	*16*	*3*	*132*	*412*
2002 Examination	*Eligible*	*261*	*83*	*49*	*6*	*370*	*769*
Between 1997 and	New to Study	--	--	--	--	317	317
2002 Examinations	No Health-Match in 1997	--	--	--	--	(91)	(91)
	Deceased	(10)	(4)	(3)	(1)	(25)	(43)
	Discovered to be Ineligible	(0)	(0)	(0)	(0)	(1)	(1)
	Remaining Eligible	*251*	*79*	*46*	*5*	*570*	*951*
	Unlocatable	(1)	(1)	(1)	(2)	(20)	(25)
	No Health-Match	--	--	--	--	(60)	(60)
	Refused	(41)	(51)	(32)	(2)	(303)	(429)
	Fully Compliant	*209*	*27*	*13*	*1*	*187*	*437*

FC	=	Fully Compliant at Baseline Examination	UNL =	Unlocatable at Baseline Examination
PC	=	Partially Compliant at Baseline Examination	NS =	New to Study Since Baseline Examination
R	=	Refusal at Baseline Examination	-- =	Undefined Categories

AIR FORCE HEALTH STUDY 2002
FOLLOW-UP EXAMINATION
SCHEDULING & REPLACEMENT
ALGORITHM

31 MAY 2001

C-5

APPENDIX D

APPENDIX D. COEFFICIENTS OF VARIATION FOR LABORATORY QUALITY CONTROL

This appendix contains a table of the coefficients of variation for each of 54 laboratory quality control assays. Included in this table are the target coefficients of variation and actual coefficients of variation. The targets are given for low, medium, and high level controls. "Target" coefficients of variation are those coefficients of variation sought be the Air Force, based on currently available lab methods. "Actual" coefficients of variation are those coefficients of variation actually achieved during the period of time given in the column labeled "Time Period" for Low, Medium, and High control levels. A different time period is given when the control lot for at least one of the levels was changed. If a control lot covers more than one time period, as listed in separate rows of the table, the coefficient of variation is repeated and annotated with an asterisk (*). The asterisk notes that a single coefficient of variation covers the adjacent time periods.

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Table D-1. Coefficients of Variation for Laboratory Quality Control–Tri-level Control Data for the 2002 Air Force Health Study Follow-up Examination Assays Performed at Scripps Clinic

Assay (Units)	Time Period	Target			Actual		
		Low	Med.	High	Low	Med.	High
2-hour Postprandial Glucose (mg/dL)	05/06/2002-09/04/2002	4.2	3.9	3.9	1.5	1.8	1.4
	09/05/2002-03/31/2003	4.2	3.9	3.9	2.6	2.3	1.9
Alkaline Phosphatase (U/L)	05/06/2002-09/04/2002	13.5	10.1	10.0	12.6	8.8	7.4
	09/05/2002-01/20/2003	13.5	10.1	10.0*	13.0	7.2	5.6*
	01/21/2003-03/31/2003	10.6	9.6	10.0*	8.2	4.9	5.6*
ALT (U/L)	05/06/2002-09/04/2002	5.3	5.2	5.1	3.8	2.2	1.9
	09/05/2002-03/31/2003	5.3	5.2	5.1	3.0	2.0	2.1
Amylase (U/L)	05/06/2002-09/04/2002	2.9	3.0	3.0	1.3	0.8	0.8
	09/05/2002-03/31/2003	2.9	3.0	3.0	1.3	0.6	0.7
AST (U/L)	05/06/2002-09/04/2002	6.1	6.3	6.0	3.3	2.1	1.5
	09/05/2002-03/31/2003	6.1	6.3	6.0	4.7	3.0	2.4
Blood Urea Nitrogen (mg/dL)	05/06/2002-09/04/2002	4.7	4.8	4.6	4.1	2.4	2.0
	09/05/2002-03/31/2003	4.7	4.8	4.6	4.5	2.2	2.2
C-peptide (ng/mL)	05/06/2002-03/31/2003	14.7	14.0	15.3	13.7	11.0	8.4
Cholesterol (mg/dL)	05/06/2002-09/04/2002	2.2	2.1	2.0	1.2	1.2	1.2
	09/05/2002-01/20/2003	2.2	2.1	2.0*	1.4	1.3	2.0*
	01/21/2003-03/31/2003	2.1	2.1	2.0*	1.0	1.1	2.0*
Creatine Phosphokinase (U/L)	05/06/2002-09/04/2002	4.5	4.4	4.5	2.8	1.8	1.2
	09/05/2002-03/31/2003	4.5	4.4	4.5	3.3	2.3	1.8
Creatinine (Serum) (mg/dL)	05/06/2002-09/04/2002	5.7	3.0	3.0	4.7	2.2	1.4
	09/05/2002-11/20/2002	5.7	3.0	3.0	2.8	2.5	1.5
	11/21/2002-03/31/2003	5.3	2.9	2.9	3.6	1.9	2.0
Creatinine (Urinary) (mg/dL)	05/06/2002-11/11/2002	3.1	3.0	2.9	2.2	2.0	1.9
	11/12/2002-03/31/2003	3.2	3.3	3.1	2.3	2.8	1.9
Direct Bilirubin (mg/dL)	05/06/2002-09/04/2002	7.6	8.1	8.1	5.7	5.2	1.7
	09/05/2002-03/31/2003	7.6	8.1	8.1	5.7	3.3	3.0
Erythrocyte Sedimentation Rate (mm/hr)	05/06/2002-06/26/2002	37.5*	20.8	15.0*	18.7*	4.6	6.6*
	06/27/2002-08/19/2002	37.5*	16.7	15.0*	18.7*	14.7	6.6*
	08/20/2002-09/18/2002	40.0	20.0	20.5	23.4	25.6	16.2
	09/19/2002-12/18/2002	40.0*	16.7	17.4*	18.3*	14.7	5.5*
	12/19/2002-02/03/2003	40.0*	17.9*	17.4*	18.3*	5.8*	5.5*
	02/04/2003-03/31/2003	37.5	17.9*	15.2	17.5	5.8*	3.9
Estradiol (pg/mL)	05/06/2002-03/31/2003	6.2	12.3	14.1	5.9	7.0	9.0
Fasting Glucose (mg/dL)	05/06/2002-09/04/2002	4.2	3.9	3.9	1.3	1.4	1.5
	09/05/2002-03/31/2003	4.2	3.9	3.9	2.4	1.9	1.6
Fibrinogen (mg/dL)	05/06/2002-03/31/2003	10.6	10.3	9.8	5.4	8.0	4.4
Follicle Stimulating Hormone (mIU/mL)	05/06/2002-03/31/2003	10.4	9.8	9.1	7.5	6.5	6.4
Free Testosterone (pg/mL)	05/06/2002-03/12/2003	10.9*	10.7	10.6	12.0*	10.1	9.8
	03/13/2003-03/31/2003	10.9*	9.2	11.7	12.0*	5.1	4.7
GGT (U/L)	05/06/2002-09/04/2002	5.1	5.0	5.0	3.4	1.1	0.9
	09/05/2002-01/20/2003	5.1	5.0	5.0	3.0	1.5	1.3
	01/21/2003-03/31/2003	4.8	4.8	4.9	3.5	1.5	1.2

Table D-1. **Coefficients of Variation for Laboratory Quality Control–Tri-level Control Data for the 2002 Air Force Health Study Follow-up Examination Assays Performed at Scripps Clinic (continued)**

Assay (Units)	Time Period	Target			Actual		
		Low	Med.	High	Low	Med.	High
Glutamic Acid Decarboxylase Antibodies	05/06/2002-06/05/2002	25.0	--	14.8	8.6	--	12.5
	06/06/2002-11/20/2002	15.4	--	17.5	12.3	--	7.6
	11/21/2002-12/18/2002	15.4	--	17.5	5.1	--	6.7
	12/19/2002-02/11/2003	15.4	--	14.0	4.7	--	4.8
	02/13/2003-03/19/2003	15.4	--	14.0	7.4	--	22.2
	03/20/2003-03/31/2003	15.4	--	14.0	12.6	--	14.1
HDL Cholesterol (mg/dL)	05/06/2002-09/04/2002	4.0	4.1	4.1	4.3	3.7	3.5
	09/05/2002-03/31/2003	4.0	4.1	4.1	3.2	3.1	2.7
Hematocrit (percent)	05/06/2002-06/26/2002	5.6	3.0	3.1	2.5	1.4	1.2
	06/27/2002-08/28/2002	5.6	3.1	3.0	2.6	1.7	1.4
	08/29/2002-10/30/2002	5.8	3.0	3.0	1.5	1.0	1.1
	10/31/2002-12/18/2002	5.5	3.0	3.0	2.9	1.0	1.2
	12/19/2002-02/26/2003	5.7	3.0	3.0	1.2	1.0	0.9
	02/27/2003-03/31/2003	5.6	3.0	3.0	2.6	1.9	1.7
Hemoglobin (g/dL)	05/06/2002-06/26/2002	2.7	1.8	2.1	0.7	0.5	0.6
	06/27/2002-08/28/2002	2.7	1.9	2.1	0.9	0.7	0.7
	08/29/2002-10/30/2002	2.8	1.8	2.0	1.5	0.7	0.5
	10/31/2002-12/18/2002	2.6	1.8	2.0	0.8	0.4	0.3
	12/19/2002-02/26/2003	2.7	1.8	2.1	0.7	0.5	0.6
	02/27/2003-03/31/2003	2.6	1.8	2.0	0.6	0.5	0.4
Hemoglobin A1c (percent)	05/06/2002-02/26/2003	3.6	2.7*	3.1	2.9	2.9*	2.7
	02/27/2003-03/31/2003	3.8	2.7*	3.2	2.1	2.9*	2.0
IgA (mg/dL)	05/08/2002-03/31/2003	9.8	9.6	9.4	5.1	5.2	5.5
IgG (mg/dL)	05/08/2002-03/31/2003	9.9	9.6	9.5	7.8	6.1	5.7
IgM (mg/dL)	05/08/2002-03/31/2003	9.7	8.8	9.0	6.7	6.6	6.5
Insulin (2-hour Postprandial And Fasting) (μIU/mL)	05/06/2002-11/04/2002	13.0	12.0	12.1	9.4	6.0	7.0
	11/05/2002-03/31/2003	14.4	13.1	13.5	8.8	5.5	5.9
Lactate Dehydrogenase (U/L)	05/06/2002-08/28/2002	3.1	3.0	3.1	2.7	2.1	2.1
	08/29/2002-12/02/2002	2.9	2.9	2.9	2.3	2.2	1.9
	12/03/2002-02/26/2003	3.1	3.0	3.1*	2.6	2.6	1.9*
	02/27/2003-03/31/2003	3.2	3.1	3.1*	2.8	1.6	1.9*
Luteinizing Hormone (mIU/mL)	05/06/2002-03/31/2003	8.3	10.6	10.1	8.0	6.0	6.6
Microalbumin (Quantitative) (mg/dL)	05/06/2002-03/31/2003	24.1	11.1	9.6	16.6	8.8	6.8
Platelet Count (thousand/mm^3)	05/06/2002-06/26/2002	14.1	6.6	5.6	6.3	3.4	3.5
	06/27/2002-08/28/2002	13.2	6.7	5.5	11.7	4.5	3.2
	08/29/2002-10/30/2002	13.6	6.8	5.5	7.1	6.3	3.9
	10/31/2002-12/18/2002	12.7	6.7	5.8	2.7	3.4	4.7
	12/19/2002-02/26/2003	14.1	6.9	6.0	3.8	4.4	5.1
	02/27/2003-03/31/2003	13.8	7.0	5.4	5.8	4.7	2.8
Prostate Specific Antigen (ng/mL)	05/06/2002-03/31/2003	16.2	16.7	21.9	10.1	5.8	6.2
Protein Profile – Albumin (g/dL)	05/06/2002-09/04/2002	4.3	3.9	4.1	2.3	1.2	1.1
	09/05/2002-03/31/2003	4.3	3.9	4.1	2.1	1.3	1.1
Protein Profile – α-1-Antitrypsin (mg/dL)	05/08/2002-03/31/2003	10.4	9.8	10.2	7.6	7.3	7.6
Protein Profile – α-1-Glycoprotein (mg/dL)	05/08/2002-03/31/2003	9.5	10.4	9.6	4.7	5.0	5.1
Protein Profile – α-2-Macroglobulin (mg/dL)	05/08/2002-03/31/2003	10.8	9.8	10.8	6.9	7.2	7.7
Protein Profile – Apolipoprotein B (mg/dL)	05/08/2002-03/31/2003	9.5	9.8	10.8	7.6	7.3	7.2
Protein Profile – C3 Complement (mg/dL)	05/08/2002-03/31/2003	9.2	9.1	9.2	6.9	6.5	6.9
Protein Profile – C4 Complement (mg/dL)	05/08/2002-03/31/2003	11.0	9.2	9.2	6.9	7.4	7.3

Table D-1. Coefficients of Variation for Laboratory Quality Control–Tri-level Control Data for the 2002 Air Force Health Study Follow-up Examination Assays Performed at Scripps Clinic (continued)

Assay (Units)	Time Period	Target			Actual		
		Low	Med.	High	Low	Med.	High
Protein Profile – Haptoglobin (mg/dL)	05/08/2002-03/31/2003	10.1	9.6	9.8	5.1	5.2	5.1
Protein Profile – Prealbumin (mg/dL)	05/08/2002-03/31/2003	10.6	9.9	9.8	4.6	5.5	4.6
Protein Profile – Transferrin (mg/dL)	05/08/2002-03/31/2003	9.7	9.7	9.6	6.8	7.2	7.1
Prothrombin Time (seconds)	05/06/2002-03/31/2003	5.0	5.0	5.1	1.8	2.5	4.0
Red Blood Cell Count (million/mm^3)	05/06/2002-06/26/2002	4.2	2.1	2.3	2.0	1.0	0.9
	06/27/2002-08/28/2002	4.2	2.2	2.2	2.3	1.5	1.3
	08/29/2002-10/30/2002	4.4	2.1	2.2	2.0	1.1	1.1
	10/31/2002-12/18/2002	4.3	2.1	2.2	2.8	1.0	1.1
	12/19/2002-02/26/2003	4.4	2.1	2.3	1.0	0.8	0.7
	02/27/2003-03/31/2003	4.3	2.2	2.2	2.6	1.6	1.8
Thyroid – Free T$_3$ (pg/mL)	05/06/2002-03/31/2003	10.0	10.4	10.6	7.1	4.4	6.7
Thyroid – Free T$_4$ (ng/dL)	05/06/2002-03/31/2003	10.0	9.1	10.0	9.5	7.7	8.2
Thyroid-Stimulating Hormone (μIU/mL)	05/06/2002-03/31/2003	9.9	9.8	9.9	6.7	5.9	6.3
Total Bilirubin (mg/dL)	05/06/2002-09/04/2002	4.0	4.1	4.3	1.5	1.7	0.8
	09/05/2002-01/08/2003	4.0	4.1*	4.3*	1.9	1.8*	1.0*
	01/09/2003-03/31/2003	7.0	4.1*	4.3*	6.8	1.8*	1.0*
Total Testosterone (ng/dL)	05/06/2002-03/31/2003	11.1	9.2	9.5	8.8	9.4	9.1
Triglycerides (mg/dL)	05/06/2002-07/29/2002	4.0	4.1*	4.0*	4.1	3.8*	2.3*
	07/30/2002-09/04/2002	4.3	4.1*	4.0*	3.5	3.8*	2.3*
	09/05/2002-01/20/2003	4.3	4.1*	4.0*	2.4	2.9*	2.4*
	01/21/2003-03/31/2003	4.1	4.1*	4.0*	3.4	2.9*	2.4*
Uric Acid (mg/dL)	05/06/2002-09/04/2002	2.7	2.5	2.9	1.7	1.3	1.2
	09/05/2002-03/31/2003	2.7	2.5	2.9	1.8	1.3	1.2
Urine Specific Gravity	05/06/2002-03/05/2003	0.3	0.3	0.3*	0.1	0.1	0.1*
	03/06/2003-03/31/2003	0.3	0.3	0.3*	0.1	0.1	0.1*
White Blood Cell Count (thousand/mm^3)	05/06/2002-06/26/2002	7.4	4.3	5.0	4.8	2.2	3.0
	06/27/2002-08/28/2002	6.8	4.7	4.8	3.4	2.3	1.9
	08/29/2002-10/30/2002	6.3	5.0	5.0	3.1	2.0	1.5
	10/31/2002-12/18/2002	4.8	4.8	5.2	3.9	3.0	1.8
	12/19/2002-02/26/2003	6.1	4.9	4.9	3.8	2.0	1.7
	02/27/2003-03/31/2003	6.3	4.7	4.9	3.7	1.8	1.3

APPENDIX E

List of Tables

Table E-1. Approximate Power to Detect an Initial Dioxin Effect at a 5-Percent Level of Significance (Discrete Dependent Variable)

Prevalence of Condition	Relative Risk								
	1.10	1.20	1.30	1.40	1.50	1.75	2.00	10.00	20.00
0.005	0.05	0.07	0.09	0.12	0.16	0.31	0.50	1.00	1.00
0.01	0.06	0.08	0.13	0.19	0.27	0.52	0.76	1.00	1.00
0.02	0.07	0.12	0.20	0.32	0.46	0.78	0.94	1.00	1.00
0.03	0.07	0.15	0.28	0.44	0.61	0.90	0.98	1.00	1.00
0.04	0.08	0.18	0.35	0.54	0.72	0.95	1.00	1.00	1.00
0.05	0.09	0.22	0.41	0.62	0.80	0.98	1.00	1.00	1.00
0.10	0.13	0.35	0.64	0.86	0.96	1.00	1.00	1.00	1.00
0.15	0.16	0.46	0.77	0.94	0.99	1.00	1.00	1.00	1.00
0.20	0.19	0.54	0.85	0.97	1.00	1.00	1.00	1.00	1.00

Table E-2. Approximate Power to Detect a Categorized Dioxin Effect (Low and High Ranch Hands Combined vs. Comparisons) at a 5-Percent Level of Significance (Discrete Dependent Variable)

Prevalence of Condition	Relative Risk								
	1.10	1.20	1.30	1.40	1.50	1.75	2.00	10.00	20.00
0.005	0.05	0.06	0.06	0.07	0.09	0.12	0.17	0.95	1.00
0.01	0.05	0.06	0.08	0.10	0.12	0.20	0.29	1.00	1.00
0.02	0.06	0.08	0.11	0.14	0.19	0.34	0.50	1.00	1.00
0.03	0.06	0.09	0.13	0.19	0.26	0.47	0.66	1.00	1.00
0.04	0.06	0.10	0.16	0.24	0.33	0.57	0.77	1.00	1.00
0.05	0.07	0.11	0.19	0.28	0.39	0.66	0.85	1.00	1.00
0.10	0.08	0.17	0.31	0.47	0.63	0.90	0.98	1.00	1.00
0.15	0.09	0.22	0.41	0.61	0.77	0.97	1.00	1.00	1.00
0.20	0.10	0.26	0.48	0.70	0.85	0.99	1.00	1.00	1.00

Table E-3. Approximate Power to Detect a Lipid-adjusted 1987 Dioxin Effect at a 5-Percent Level of Significance (Discrete Dependent Variable)

Prevalence of Condition	Relative Risk								
	1.10	1.20	1.30	1.40	1.50	1.75	2.00	10.00	20.00
0.005	0.06	0.09	0.15	0.23	0.34	0.64	0.88	1.00	1.00
0.01	0.07	0.14	0.25	0.40	0.57	0.90	0.99	1.00	1.00
0.02	0.09	0.23	0.44	0.67	0.84	0.99	1.00	1.00	1.00
0.03	0.12	0.31	0.59	0.82	0.95	1.00	1.00	1.00	1.00
0.04	0.14	0.39	0.70	0.91	0.98	1.00	1.00	1.00	1.00
0.05	0.16	0.46	0.79	0.95	0.99	1.00	1.00	1.00	1.00
0.10	0.26	0.72	0.96	1.00	1.00	1.00	1.00	1.00	1.00
0.15	0.34	0.85	0.99	1.00	1.00	1.00	1.00	1.00	1.00
0.20	0.41	0.91	1.00	1.00	1.00	1.00	1.00	1.00	1.00

Table E-4. Approximate Power to Detect an Initial Dioxin Effect at a 5-Percent Level of Significance (Continuous Dependent Variable)

Mean Change	Coefficient of Variation ($100\ \sigma/\mu$)					
	5	10	15	25	50	75
0.005	0.78	0.28	0.15	0.09	0.06	0.05
0.01	1.00	0.78	0.45	0.19	0.09	0.07
0.02	1.00	1.00	0.95	0.59	0.19	0.11
0.03	1.00	1.00	1.00	0.91	0.38	0.19
0.04	1.00	1.00	1.00	0.99	0.59	0.31
0.05	1.00	1.00	1.00	1.00	0.78	0.45
0.10	1.00	1.00	1.00	1.00	1.00	0.95

Table E-5. Approximate Power to Detect a Categorized Dioxin Effect (Low plus High Ranch Hands vs. Comparisons) at a 5-Percent Level of Significance (Continuous Dependent Variable)

Mean Change	Coefficient of Variation (100 σ/μ)					
	5	10	15	25	50	75
0.005	0.42	0.14	0.09	0.06	0.05	0.05
0.01	0.94	0.42	0.22	0.11	0.06	0.06
0.02	1.00	0.94	0.65	0.29	0.11	0.08
0.03	1.00	1.00	0.94	0.56	0.19	0.11
0.04	1.00	1.00	1.00	0.81	0.29	0.16
0.05	1.00	1.00	1.00	0.94	0.42	0.22
0.10	1.00	1.00	1.00	1.00	0.94	0.65

Table E-6. Approximate Power to Detect a Lipid-adjusted 1987 Dioxin Effect at a 5-Percent Level of Significance (Continuous Dependent Variable)

Mean Change	Coefficient of Variation (100 σ/μ)					
	5	10	15	25	50	75
0.005	0.99	0.61	0.32	0.15	0.07	0.06
0.01	1.00	0.99	0.85	0.43	0.15	0.09
0.02	1.00	1.00	1.00	0.95	0.43	0.22
0.03	1.00	1.00	1.00	1.00	0.77	0.43
0.04	1.00	1.00	1.00	1.00	0.95	0.67
0.05	1.00	1.00	1.00	1.00	0.99	0.85
0.10	1.00	1.00	1.00	1.00	1.00	1.00

APPENDIX F

APPENDIX F. DEPENDENT VARIABLE-COVARIATE ASSOCIATIONS

This appendix contains results of tests of association between each dependent variable and covariates for the adjusted analysis of each dependent variable. Pearson's chi-square test (continuity-adjusted for 2x2 tables) is used for significance testing of the associations between each discrete dependent variable and the covariate (see Chapter 7, Table 7-5). When a covariate is continuous in nature (e.g., age), the covariate is put in its discrete form prior to the analysis of the discrete dependent variable. Pearson's correlation coefficient is used for significance testing of the associations between each continuous dependent variable and a continuous covariate (see Chapter 7, Table 7-5). When a covariate is discrete in nature, means (transformed back to the original scale, if necessary) are presented and an analysis of variance is used to investigate the difference between the means (see Chapter 7, Table 7-5).

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Table F-1. Dependent Variable-covariate Associations for the General Health Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Self-perception of Health		(n=889)	(n=1,060)		(n=125)	(n=1,824)	
	Fair or Poor	12.6%	14.7%	0.198	14.4%	13.7%	0.933
Appearance of Illness or Distress		(n=890)	(n=1,060)		(n=125)	(n=1,825)	
	Yes	2.0%	5.9%	<0.001	6.4%	4.0%	0.285
Relative Age Appearance		(n=890)	(n=1,060)		(n=125)	(n=1,825)	
	Older	5.3%	4.1%	0.240	2.4%	4.8%	0.317
Body Mass Index		(n=890)	(n=1,060)		(n=125)	(n=1,825)	
(continuous)[a]	--	r = -0.068		0.003	$\bar{O}$ = 29.26	$\bar{O}$ = 28.65	0.121
(discrete)	Obese (>30 kg/m^2)	37.3%	33.7%	0.105	42.4%	34.9%	0.107

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Self-perception of Health		(n=769)	(n=318)	(n=862)	
	Fair or Poor	8.2%	18.6%	16.9%	<0.001
Appearance of Illness or Distress		(n=768)	(n=318)	(n=864)	
	Yes	3.9%	6.0%	3.7%	0.201
Relative Age Appearance		(n=768)	(n=318)	(n=864)	
	Older	1.7%	9.4%	5.4%	<0.001
Body Mass Index		(n=768)	(n=318)	(n=864)	
(continuous)[a]	--	$\bar{O}$ = 29.01	$\bar{O}$ = 28.72	$\bar{O}$ = 29.01	0.003
(discrete)	Obese (>30 kg/m^2)	30.2%	36.5%	39.5%	<0.001

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				
		Never	Former	>0–20	>20	p-Value
Self-perception of Health		(n=601)	(n=1,076)	(n=214)	(n=58)	
	Fair or Poor	10.3%	13.0%	21.0%	36.2%	<0.001
Appearance of Illness or Distress		(n=601)	(n=1,075)	(n=214)	(n=58)	
	Yes	2.0%	4.7%	6.1%	8.6%	0.005
Relative Age Appearance		(n=601)	(n=1,075)	(n=214)	(n=58)	
	Older	2.5%	3.8%	10.3%	20.7%	<0.001
Body Mass Index		(n=601)	(n=1,075)	(n=214)	(n=58)	
(continuous)[a]	--	r = -0.141				<0.001
(discrete)	Obese (>30 kg/m^2)	35.9%	38.0%	25.2%	19.0%	<0.001

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	>0–10	>10	p-Value
Self-perception of Health		(n=601)	(n=491)	(n=856)	
	Fair or Poor	10.3%	9.2%	18.8%	<0.001
Appearance of Illness or Distress		(n=601)	(n=491)	(n=855)	
	Yes	2.0%	4.1%	5.6%	0.003
Relative Age Appearance		(n=601)	(n=491)	(n=855)	
	Older	2.5%	2.7%	7.3%	<0.001
Body Mass Index		(n=601)	(n=491)	(n=855)	
(continuous)[a]			r = -0.001		0.964
(discrete)	Obese (>30 kg/m^2)	35.9%	33.4%	36.0%	0.584

Dependent Variable	Level	Current Alcohol Use (drinks/day)		
		0–1	>1	p-Value
Self-perception of Health		(n=1,657)	(n=292)	
	Fair or Poor	14.1%	11.6%	0.298
Appearance of Illness or Distress		(n=1,656)	(n=292)	
	Yes	3.9%	5.5%	0.262
Relative Age Appearance		(n=1,656)	(n=292)	
	Older	4.6%	4.8%	0.998
Body Mass Index		(n=1,656)	(n=292)	
(continuous)[a]		r = -0.091		<0.001
(discrete)	Obese (>30 kg/m^2)	36.2%	30.8%	0.090

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	>0–40	>40	p-Value
Self-perception of Health		(n=107)	(n=1,234)	(n=601)	
	Fair or Poor	20.6%	12.2%	15.5%	0.018
Appearance of Illness or Distress		(n=107)	(n=1,233)	(n=601)	
	Yes	2.8%	3.7%	5.2%	0.275
Relative Age Appearance		(n=107)	(n=1,233)	(n=601)	
	Older	4.7%	4.1%	5.7%	0.348
Body Mass Index		(n=107)	(n=1,233)	(n=601)	
(continuous)[a]			r = -0.059		0.010
(discrete)	Obese (>30 kg/m^2)	37.4%	36.5%	32.5%	0.210

[a]Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.

Note: Correlations (r) are based on total sample size and are not category-specific.

Please see Section 9.1.3 and Table 9-1 for a further discussion of the dependent variables and covariates shown in this appendix.

Table F-2. Dependent Variable-covariate Associations for the Neoplasia Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Any Skin Neoplasm		(n=814)	(n=993)				
	Yes	42.9%	56.5%	<0.001	--	--	--
Malignant Skin Neoplasm		(n=814)	(n=993)				
	Yes	14.9%	29.8%	<0.001	--	--	--
Benign Skin Neoplasm		(n=885)	(n=1,046)				
	Yes	33.3%	38.0%	0.039	--	--	--
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=814) 0.4%	(n=993) 1.0%	0.188	--	--	--
Basal Cell Carcinoma		(n=814)	(n=993)				
	Yes	12.0%	24.1%	<0.001	--	--	--
Squamous Cell Carcinoma		(n=814)	(n=993)				
	Yes	2.5%	8.7%	<0.001	--	--	--
Nonmelanoma		(n=814)	(n=993)				
	Yes	13.4%	28.1%	<0.001	--	--	--
Melanoma		(n=814)	(n=993)				
	Yes	1.6%	3.7%	0.009	--	--	--
Any Systemic Neoplasm		(n=886)	(n=1,049)		(n=124)	(n=1,811)	
	Yes	23.1%	42.5%	<0.001	29.0%	34.0%	0.305
Malignant Systemic Neoplasm		(n=888)	(n=1,053)		(n=124)	(n=1,817)	
	Yes	4.7%	16.4%	<0.001	11.3%	11.1%	0.999
Benign Systemic Neoplasm		(n=886)	(n=1,049)		(n=124)	(n=1,811)	
	Yes	18.5%	30.7%	<0.001	19.4%	25.5%	0.155
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=888) 1.7%	(n=1,053) 2.4%	0.369	(n=124) 0.8%	(n=1,817) 2.2%	0.491
Malignant Systemic Neoplasm of the Eye, Ear, Face, Head, or Neck	Yes	(n=888) 0.3%	(n=1,053) 0.2%	0.849	(n=124) 0.0%	(n=1,817) 0.3%	0.999
Malignant Systemic Neoplasm of the Oral Cavity, Pharynx, or Larynx	Yes	(n=888) 0.3%	(n=1,053) 1.0%	0.172	(n=124) 0.8%	(n=1,817) 0.7%	0.999
Malignant Systemic Neoplasm of the Thymus or Mediastinum	Yes	(n=888) 0.2%	(n=1,053) 0.1%	0.882	(n=124) 0.0%	(n=1,817) 0.2%	0.999
Malignant Systemic Neoplasm of the Thyroid Gland	Yes	(n=888) 0.0%	(n=1,053) 0.3%	0.312	(n=124) 0.0%	(n=1,817) 0.2%	0.999
Malignant Systemic Neoplasm of the Bronchus or Lung	Yes	(n=888) 0.5%	(n=1,053) 1.5%	0.036	(n=124) 0.0%	(n=1,817) 1.1%	0.475
Any Systemic Neoplasm of the Stomach	Yes	(n=888) 0.5%	(n=1,053) 1.0%	0.305	(n=124) 0.8%	(n=1,817) 0.7%	0.999
Malignant Systemic Neoplasm of the Colon or Rectum	Yes	(n=888) 0.9%	(n=1,053) 1.3%	0.501	(n=124) 0.8%	(n=1,817) 1.2%	0.999

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Malignant Systemic Neoplasm of the Urinary System	Yes	(n=888) 0.5%	(n=1,053) 2.5%	<0.001	(n=124) 0.8%	(n=1,817) 1.6%	0.754
Malignant Systemic Neoplasm of the Kidney or Ureter	Yes	(n=888) 0.2%	(n=1,053) 0.9%	0.124	(n=124) 0.8%	(n=1,817) 0.6%	0.999
Malignant Systemic Neoplasm of the Prostate	Yes	(n=888) 1.7%	(n=1,053) 10.0%	<0.001	(n=124) 9.7%	(n=1,817) 5.9%	0.140
Malignant Systemic Neoplasm of the Penis or Other Male Genital Organs	Yes	(n=888) 0.0%	(n=1,053) 0.2%	0.556	(n=124) 0.0%	(n=1,817) 0.1%	0.999
Malignant Systemic Neoplasm of the Testicles	Yes	(n=888) 0.0%	(n=1,053) 0.3%	0.312	(n=124) 0.0%	(n=1,817) 0.2%	0.999
Malignant Systemic Neoplasm of Bone or Articular Cartilage	Yes	(n=888) 0.1%	(n=1,053) 0.3%	0.740	(n=124) 0.0%	(n=1,817) 0.2%	0.999
Malignant Systemic Neoplasm of Connective or Other Soft Tissues	Yes	(n=888) 0.3%	(n=1,053) 0.4%	0.999	(n=124) 0.0%	(n=1,817) 0.4%	0.999
Carcinoma in Situ	Yes	(n=888) 0.2%	(n=1,053) 0.8%	0.187	(n=124) 0.0%	(n=1,817) 0.6%	0.857
Hodgkin's Disease	Yes	(n=888) 0.1%	(n=1,053) 0.1%	0.999	(n=124) 0.0%	(n=1,817) 0.1%	0.999
Leukemia	Yes	(n=888) 0.5%	(n=1,053) 0.6%	0.962	(n=124) 0.0%	(n=1,817) 0.6%	0.857
Other Malignant Systemic Neoplasms of Lymphoid or Histiocytic Tissue	Yes	(n=888) 0.2%	(n=1,053) 1.2%	0.023	(n=124) 0.0%	(n=1,817) 0.8%	0.627
Lymphoreticular Sarcoma	Yes	(n=888) 0.1%	(n=1,053) 0.3%	0.740	(n=124) 0.0%	(n=1,817) 0.2%	0.999
Skin or Systemic Neoplasm	Yes	(n=881) 53.8%	(n=1,035) 71.8%	<0.001	(n=123) 52.0%	(n=1,793) 64.3%	0.008
Malignant Skin or Systemic Neoplasm	Yes	(n=883) 17.3%	(n=1,038) 39.1%	<0.001	(n=123) 11.4%	(n=1,798) 30.3%	<0.001
PSA (ng/mL)		(n=871)	(n=932)		(n=111)	(n=1,692)	
(continuous)[a]	--	r = 0.229		<0.001	O = 1.08	O = 0.96	0.123
(discrete)	High	2.1%	7.7%	<0.001	3.6%	5.1%	0.640

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Any Skin Neoplasm	Yes	(n=744) 53.8%	(n=293) 53.2%	(n=770) 46.0%	0.006
Malignant Skin Neoplasm	Yes	(n=744) 28.0%	(n=293) 25.3%	(n=770) 17.5%	<0.001
Benign Skin Neoplasm	Yes	(n=758) 36.3%	(n=315) 36.8%	(n=858) 35.1%	0.814

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=744) 1.1%	(n=293) 0.0%	(n=770) 0.7%	0.174
Basal Cell Carcinoma	Yes	(n=744) 22.9%	(n=293) 20.1%	(n=770) 14.0%	<0.001
Squamous Cell Carcinoma	Yes	(n=744) 8.1%	(n=293) 5.8%	(n=770) 3.8%	0.002
Nonmelanoma	Yes	(n=744) 26.1%	(n=293) 24.2%	(n=770) 16.0%	<0.001
Melanoma	Yes	(n=744) 3.8%	(n=293) 2.1%	(n=770) 2.1%	0.097
Any Systemic Neoplasm	Yes	(n=760) 37.8%	(n=314) 35.0%	(n=861) 29.5%	0.002
Malignant Systemic Neoplasm	Yes	(n=763) 13.1%	(n=316) 14.6%	(n=862) 8.0%	<0.001
Benign Systemic Neoplasm	Yes	(n=760) 28.0%	(n=314) 23.9%	(n=861) 23.0%	0.057
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=763) 2.6%	(n=316) 1.6%	(n=862) 1.7%	0.371
Malignant Systemic Neoplasm of the Eye, Ear, Face, Head, or Neck	Yes	(n=763) 0.1%	(n=316) 0.6%	(n=862) 0.2%	0.328
Malignant Systemic Neoplasm of the Oral Cavity, Pharynx, or Larynx	Yes	(n=763) 0.5%	(n=316) 1.6%	(n=862) 0.5%	0.093
Malignant Systemic Neoplasm of the Thymus or Mediastinum	Yes	(n=763) 0.1%	(n=316) 0.3%	(n=862) 0.1%	0.724
Malignant Systemic Neoplasm of the Thyroid Gland	Yes	(n=763) 0.3%	(n=316) 0.0%	(n=862) 0.1%	0.564
Malignant Systemic Neoplasm of the Bronchus or Lung	Yes	(n=763) 1.2%	(n=316) 1.9%	(n=862) 0.6%	0.121
Any Systemic Neoplasm of the Stomach	Yes	(n=763) 0.8%	(n=316) 1.3%	(n=862) 0.5%	0.341
Malignant Systemic Neoplasm of the Colon or Rectum	Yes	(n=763) 1.4%	(n=316) 1.3%	(n=862) 0.8%	0.475
Malignant Systemic Neoplasm of the Urinary System	Yes	(n=763) 1.7%	(n=316) 1.6%	(n=862) 1.4%	0.877
Malignant Systemic Neoplasm of the Kidney or Ureter	Yes	(n=763) 0.4%	(n=316) 0.3%	(n=862) 0.8%	0.432
Malignant Systemic Neoplasm of the Prostate	Yes	(n=763) 7.5%	(n=316) 7.6%	(n=862) 4.5%	0.025
Malignant Systemic Neoplasm of the Penis or Other Male Genital Organs	Yes	(n=763) 0.0%	(n=316) 0.6%	(n=862) 0.0%	0.006

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Malignant Systemic Neoplasm of the Testicles		(n=763)	(n=316)	(n=862)	
	Yes	0.1%	0.3%	0.1%	0.724
Malignant Systemic Neoplasm of Bone or Articular Cartilage		(n=763)	(n=316)	(n=862)	
	Yes	0.1%	0.6%	0.1%	0.188
Malignant Systemic Neoplasm of Connective or Other Soft Tissues		(n=763)	(n=316)	(n=862)	
	Yes	0.4%	0.6%	0.2%	0.585
Carcinoma in Situ		(n=763)	(n=316)	(n=862)	
	Yes	0.4%	1.6%	0.2%	0.014
Hodgkin's Disease		(n=763)	(n=316)	(n=862)	
	Yes	0.1%	0.0%	0.1%	0.820
Leukemia		(n=763)	(n=316)	(n=862)	
	Yes	0.9%	0.3%	0.2%	0.135
Other Malignant Systemic Neoplasms of Lymphoid or Histiocytic Tissue		(n=763)	(n=316)	(n=862)	
	Yes	0.7%	1.6%	0.6%	0.196
Lymphoreticular Sarcoma		(n=763)	(n=316)	(n=862)	
	Yes	0.5%	0.0%	0.0%	0.045
Skin or Systemic Neoplasm		(n=750)	(n=311)	(n=855)	
	Yes	68.4%	67.9%	57.7%	<0.001
Malignant Skin or Systemic Neoplasm		(n=752)	(n=313)	(n=856)	
	Yes	35.5%	33.2%	22.0%	<0.001
PSA (ng/mL)		(n=692)	(n=288)	(n=823)	
(continuous)[a]	--	O = 1.05	O = 1.06	O = 0.86	<0.001
(discrete)	High	6.8%	5.2%	3.4%	0.010

Dependent Variable	Level	Body Mass Index (kg/m^2)			Cumulative Ionizing Radiation Exposure		
		Not Obese (≤30)	Obese (>30)	p-Value	Yes	No	p-Value
Any Skin Neoplasm		(n=1,176)	(n=630)		(n=437)	(n=1,370)	
	Yes	50.0%	51.0%	0.737	53.8%	49.3%	0.113
Malignant Skin Neoplasm		(n=1,176)	(n=630)		(n=437)	(n=1,370)	
	Yes	23.0%	23.0%	0.999	24.3%	22.7%	0.544
Benign Skin Neoplasm		(n=1,247)	(n=683)		(n=476)	(n=1,455)	
	Yes	35.2%	37.0%	0.450	38.7%	34.9%	0.155
Skin Neoplasm of Uncertain Behavior or Unspecified Nature		(n=1,176)	(n=630)		(n=437)	(n=1,370)	
	Yes	0.6%	1.0%	0.573	0.7%	0.7%	0.999
Basal Cell Carcinoma		(n=1,176)	(n=630)		(n=437)	(n=1,370)	
	Yes	18.5%	18.9%	0.870	18.5%	18.7%	0.999
Squamous Cell Carcinoma		(n=1,176)	(n=630)		(n=437)	(n=1,370)	
	Yes	6.1%	5.4%	0.603	5.7%	5.9%	0.975

Dependent Variable	Level	Body Mass Index (kg/m^2)			Cumulative Ionizing Radiation Exposure		
		Not Obese (≤30)	Obese (>30)	p-Value	Yes	No	p-Value
Nonmelanoma		(n=1,176)	(n=630)		(n=437)	(n=1,370)	
	Yes	21.3%	21.6%	0.952	21.5%	21.5%	0.999
Melanoma		(n=1,176)	(n=630)		(n=437)	(n=1,370)	
	Yes	2.8%	2.7%	0.999	3.9%	2.4%	0.140
Any Systemic Neoplasm		(n=1,254)	(n=680)		(n=484)	(n=1,451)	
	Yes	33.3%	34.3%	0.716	36.6%	32.7%	0.129
Malignant Systemic Neoplasm		(n=1,256)	(n=684)		(n=485)	(n=1,456)	
	Yes	11.5%	10.4%	0.515	14.9%	9.8%	0.003
Benign Systemic Neoplasm		(n=1,254)	(n=680)		(n=484)	(n=1,451)	
	Yes	24.4%	26.5%	0.344	26.5%	24.7%	0.472
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=1,256) 2.1%	(n=684) 2.1%	0.999	(n=485) 1.9%	(n=1,456) 2.1%	0.855
Malignant Systemic Neoplasm of the Eye, Ear, Face, Head, or Neck	Yes	(n=1,256) 0.3%	(n=684) 0.2%	0.805	(n=485) 0.4%	(n=1,456) 0.2%	0.795
Malignant Systemic Neoplasm of the Oral Cavity, Pharynx, or Larynx	Yes	(n=1,256) 0.8%	(n=684) 0.4%	0.528	(n=485) 1.7%	(n=1,456) 0.3%	0.006
Malignant Systemic Neoplasm of the Thymus or Mediastinum	Yes	(n=1,256) 0.2%	(n=684) 0.2%	0.999	(n=485) 0.2%	(n=1,456) 0.1%	0.999
Malignant Systemic Neoplasm of the Thyroid Gland	Yes	(n=1,256) 0.2%	(n=684) 0.2%	0.999	(n=485) 0.0%	(n=1,456) 0.2%	0.739
Malignant Systemic Neoplasm of the Bronchus or Lung	Yes	(n=1,256) 0.8%	(n=684) 1.5%	0.249	(n=485) 1.9%	(n=1,456) 0.8%	0.069
Any Systemic Neoplasm of the Stomach	Yes	(n=1,256) 0.7%	(n=684) 0.7%	0.999	(n=485) 0.6%	(n=1,456) 0.8%	0.999
Malignant Systemic Neoplasm of the Colon or Rectum	Yes	(n=1,256) 0.9%	(n=684) 1.6%	0.218	(n=485) 1.2%	(n=1,456) 1.1%	0.999
Malignant Systemic Neoplasm of the Urinary System	Yes	(n=1,256) 1.5%	(n=684) 1.6%	0.999	(n=485) 2.9%	(n=1,456) 1.1%	0.011
Malignant Systemic Neoplasm of the Kidney or Ureter	Yes	(n=1,256) 0.6%	(n=684) 0.6%	0.999	(n=485) 0.8%	(n=1,456) 0.5%	0.600
Malignant Systemic Neoplasm of the Prostate	Yes	(n=1,256) 6.7%	(n=684) 5.3%	0.252	(n=485) 7.0%	(n=1,456) 5.9%	0.444
Malignant Systemic Neoplasm of the Penis or Other Male Genital Organs	Yes	(n=1,256) 0.2%	(n=684) 0.0%	0.761	(n=485) 0.4%	(n=1,456) 0.0%	0.102
Malignant Systemic Neoplasm of the Testicles	Yes	(n=1,256) 0.2%	(n=684) 0.2%	0.999	(n=485) 0.2%	(n=1,456) 0.1%	0.999
Malignant Systemic Neoplasm of Bone or Articular Cartilage	Yes	(n=1,256) 0.1%	(n=684) 0.4%	0.254	(n=485) 0.4%	(n=1,456) 0.1%	0.563
Malignant Systemic Neoplasm of Connective or Other Soft Tissues	Yes	(n=1,256) 0.3%	(n=684) 0.4%	0.980	(n=485) 0.8%	(n=1,456) 0.2%	0.126

Dependent Variable	Level	Body Mass Index (kg/m^2)			Cumulative Ionizing Radiation Exposure		
		Not Obese (≤30)	Obese (>30)	p-Value	Yes	No	p-Value
Carcinoma in Situ		(n=1,256)	(n=684)		(n=485)	(n=1,456)	
	Yes	0.6%	0.3%	0.496	0.6%	0.5%	0.999
Hodgkin's Disease		(n=1,256)	(n=684)		(n=485)	(n=1,456)	
	Yes	0.2%	0.0%	0.761	0.0%	0.1%	0.999
Leukemia		(n=1,256)	(n=684)		(n=485)	(n=1,456)	
	Yes	0.6%	0.4%	0.986	0.2%	0.6%	0.465
Other Malignant Systemic Neoplasms of Lymphoid or Histiocytic Tissue	Yes	(n=1,256) 0.7%	(n=684) 0.9%	0.909	(n=485) 1.2%	(n=1,456) 0.6%	0.294
Lymphoreticular Sarcoma		(n=1,256)	(n=684)		(n=485)	(n=1,456)	
	Yes	0.3%	0.0%	0.340	0.0%	0.3%	0.564
Skin or Systemic Neoplasm		(n=1,240)	(n=675)		(n=474)	(n=1,442)	
	Yes	63.6%	63.3%	0.912	66.5%	62.6%	0.140
Malignant Skin or Systemic Neoplasm		(n=1,242)	(n=678)		(n=475)	(n=1,446)	
	Yes	29.8%	27.7%	0.369	31.8%	28.2%	0.153
PSA (ng/mL)		(n=1,155)	(n=647)		(n=443)	(n=1,360)	
(continuous)[a]	--	r = -0.100		<0.001	Ô = 0.99	Ô = 0.95	0.325
(discrete)	High	5.3%	4.5%	0.526	6.1%	4.6%	0.271

Dependent Variable	Level	Skin Color			Hair Color		
		Nonpeach	Peach	p-Value	Black, Dark Brown	Light Brown, Blond, Red, Bald	p-Value
Any Skin Neoplasm		(n=458)	(n=1,349)		(n=1,243)	(n=564)	
	Yes	43.0%	52.9%	<0.001	49.2%	53.0%	0.142
Malignant Skin Neoplasm		(n=458)	(n=1,349)		(n=1,243)	(n=564)	
	Yes	17.9%	24.8%	0.003	20.5%	28.7%	<0.001
Benign Skin Neoplasm		(n=574)	(n=1,357)		(n=1,359)	(n=572)	
	Yes	30.7%	38.0%	0.002	36.0%	35.5%	0.877
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=458) 0.9%	(n=1,349) 0.7%	0.896	(n=1,243) 0.5%	(n=564) 1.2%	0.142
Basal Cell Carcinoma		(n=458)	(n=1,349)		(n=1,243)	(n=564)	
	Yes	15.5%	19.7%	0.053	16.9%	22.5%	0.006
Squamous Cell Carcinoma		(n=458)	(n=1,349)		(n=1,243)	(n=564)	
	Yes	3.3%	6.8%	0.009	4.7%	8.5%	0.002
Nonmelanoma		(n=458)	(n=1,349)		(n=1,243)	(n=564)	
	Yes	17.3%	22.9%	0.013	18.9%	27.1%	<0.001
Melanoma		(n=458)	(n=1,349)		(n=1,243)	(n=564)	
	Yes	1.8%	3.1%	0.169	2.3%	3.7%	0.130
Any Skin or Systemic Neoplasm		(n=570)	(n=1,346)		(n=1,351)	(n=565)	
	Yes	56.5%	66.5%	<0.001	62.0%	67.3%	0.032

Dependent Variable	Level	Skin Color			Hair Color		
		Nonpeach	Peach	p-Value	Black, Dark Brown	Light Brown, Blond, Red, Bald	p-Value
Malignant Skin or Systemic Neoplasm	Yes	(n=572) 22.6%	(n=1,349) 31.9%	<0.001	(n=1,354) 25.3%	(n=567) 38.1%	<0.001

Dependent Variable	Level	Eye Color			
		Brown	Hazel, Green	Gray, Blue	p-Value
Any Skin Neoplasm	Yes	(n=542) 44.3%	(n=498) 52.6%	(n=767) 53.2%	0.003
Malignant Skin Neoplasm	Yes	(n=542) 16.4%	(n=498) 24.1%	(n=767) 27.1%	<0.001
Benign Skin Neoplasm	Yes	(n=662) 32.9%	(n=502) 37.9%	(n=767) 37.0%	0.151
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=542) 0.0%	(n=498) 1.8%	(n=767) 0.5%	0.002
Basal Cell Carcinoma	Yes	(n=542) 14.0%	(n=498) 20.7%	(n=767) 20.6%	0.004
Squamous Cell Carcinoma	Yes	(n=542) 2.4%	(n=498) 6.6%	(n=767) 7.8%	<0.001
Nonmelanoma	Yes	(n=542) 15.5%	(n=498) 22.7%	(n=767) 24.9%	<0.001
Melanoma	Yes	(n=542) 1.7%	(n=498) 2.2%	(n=767) 3.9%	0.034
Skin or Systemic Neoplasm	Yes	(n=659) 57.2%	(n=498) 68.9%	(n=759) 65.5%	<0.001
Malignant Skin or Systemic Neoplasm	Yes	(n=660) 21.2%	(n=500) 32.6%	(n=761) 33.6%	<0.001

Dependent Variable	Level	Skin Reaction to Sun after First Exposure				
		No Reaction	Some Redness Only	Burns	Painfully Burns	p-Value
Any Skin Neoplasm	Yes	(n=587) 47.2%	(n=815) 50.6%	(n=297) 52.5%	(n=106) 60.4%	0.066
Malignant Skin Neoplasm	Yes	(n=587) 15.7%	(n=815) 24.2%	(n=297) 27.6%	(n=106) 42.5%	<0.001
Benign Skin Neoplasm	Yes	(n=688) 37.9%	(n=829) 35.1%	(n=305) 35.1%	(n=107) 30.8%	0.432
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=587) 0.9%	(n=815) 0.9%	(n=297) 0.3%	(n=106) 0.0%	0.628
Basal Cell Carcinoma	Yes	(n=587) 12.4%	(n=815) 19.3%	(n=297) 23.2%	(n=106) 34.9%	<0.001

Dependent Variable	Level	Skin Reaction to Sun after First Exposure				
		No Reaction	Some Redness Only	Burns	Painfully Burns	p-Value
Squamous Cell Carcinoma		(n=587)	(n=815)	(n=297)	(n=106)	
	Yes	3.1%	5.9%	8.8%	13.2%	<0.001
Nonmelanoma		(n=587)	(n=815)	(n=297)	(n=106)	
	Yes	14.5%	22.6%	25.9%	38.7%	<0.001
Melanoma		(n=587)	(n=815)	(n=297)	(n=106)	
	Yes	1.7%	2.7%	3.7%	6.6%	0.026
Skin or Systemic Neoplasm		(n=679)	(n=824)	(n=305)	(n=106)	
	Yes	62.0%	63.0%	64.6%	74.5%	0.091
Malignant Skin or Systemic Neoplasm		(n=682)	(n=826)	(n=305)	(n=106)	
	Yes	21.3%	31.1%	32.5%	53.8%	<0.001

Dependent Variable	Level	Skin Reaction to Sun after Repeated Exposures				
		Deep Tan	Moderate Tan	Mild Tan	Freckles	p-Value
Any Skin Neoplasm		(n=405)	(n=985)	(n=349)	(n=66)	
	Yes	45.7%	48.9%	57.0%	65.2%	0.001
Malignant Skin Neoplasm		(n=405)	(n=985)	(n=349)	(n=66)	
	Yes	14.8%	21.4%	33.2%	43.9%	<0.001
Benign Skin Neoplasm		(n=457)	(n=1,042)	(n=359)	(n=71)	
	Yes	36.5%	35.9%	35.9%	31.0%	0.843
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=405) 0.7%	(n=985) 0.8%	(n=349) 0.3%	(n=66) 1.5%	0.655
Basal Cell Carcinoma		(n=405)	(n=985)	(n=349)	(n=66)	
	Yes	12.4%	17.1%	26.4%	39.4%	<0.001
Squamous Cell Carcinoma		(n=405)	(n=985)	(n=349)	(n=66)	
	Yes	2.7%	5.2%	9.2%	18.2%	<0.001
Nonmelanoma		(n=405)	(n=985)	(n=349)	(n=66)	
	Yes	13.6%	20.1%	30.4%	42.4%	<0.001
Melanoma		(n=405)	(n=985)	(n=349)	(n=66)	
	Yes	1.5%	2.5%	4.9%	3.0%	0.038
Skin or Systemic Neoplasm		(n=454)	(n=1,032)	(n=357)	(n=71)	
	Yes	57.7%	63.4%	68.6%	77.5%	<0.001
Malignant Skin or Systemic Neoplasm		(n=455)	(n=1,036)	(n=357)	(n=71)	
	Yes	20.0%	28.0%	40.1%	47.9%	<0.001

Dependent Variable	Level	Composite Skin-reaction Index			
		Low	Medium	High	p-Value
Any Skin Neoplasm		(n=1,200)	(n=459)	(n=146)	
	Yes	47.5%	54.3%	61.6%	<0.001
Malignant Skin Neoplasm		(n=1,200)	(n=459)	(n=146)	
	Yes	18.8%	28.3%	41.1%	<0.001

Dependent Variable	Level	Composite Skin-reaction Index			
		Low	Medium	High	p-Value
Benign Skin Neoplasm		(n=1,302)	(n=475)	(n=152)	
	Yes	35.9%	36.6%	32.9%	0.702
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=1,200) 0.8%	(n=459) 0.4%	(n=146) 0.7%	0.692
Basal Cell Carcinoma		(n=1,200)	(n=459)	(n=146)	
	Yes	15.1%	22.9%	34.3%	<0.001
Squamous Cell Carcinoma		(n=1,200)	(n=459)	(n=146)	
	Yes	4.1%	7.8%	14.4%	<0.001
Nonmelanoma		(n=1,200)	(n=459)	(n=146)	
	Yes	17.5%	26.4%	38.4%	<0.001
Melanoma		(n=1,200)	(n=459)	(n=146)	
	Yes	2.2%	3.7%	4.8%	0.070
Skin or Systemic Neoplasm		(n=1,289)	(n=474)	(n=151)	
	Yes	61.1%	66.7%	74.8%	0.001
Malignant Skin or Systemic Neoplasm		(n=1,294)	(n=474)	(n=151)	
	Yes	24.9%	34.4%	48.3%	<0.001

Dependent Variable	Level	Average Lifetime Residential History			Cumulative Industrial Chemicals Exposure		
		<37°	≥37°	p-Value	Yes	No	p-Value
Any Skin Neoplasm		(n=925)	(n=878)		(n=1,119)	(n=688)	
	Yes	52.7%	48.0%	0.052	50.4%	50.3%	0.999
Malignant Skin Neoplasm		(n=925)	(n=878)		(n=1,119)	(n=688)	
	Yes	26.5%	19.6%	<0.001	22.5%	24.0%	0.510
Benign Skin Neoplasm		(n=1,002)	(n=925)		(n=1,203)	(n=728)	
	Yes	35.0%	36.7%	0.488	35.8%	35.9%	0.999
Skin Neoplasm of Uncertain Behavior or Unspecified Nature	Yes	(n=925) 0.8%	(n=878) 0.7%	0.999	(n=1,119) 0.5%	(n=688) 1.2%	0.144
Basal Cell Carcinoma		(n=925)	(n=878)		(n=1,119)	(n=688)	
	Yes	22.2%	15.0%	<0.001	18.5%	18.9%	0.882
Squamous Cell Carcinoma		(n=925)	(n=878)		(n=1,119)	(n=688)	
	Yes	7.4%	4.3%	0.009	5.2%	7.0%	0.141
Nonmelanoma		(n=925)	(n=878)		(n=1,119)	(n=688)	
	Yes	25.3%	17.5%	<0.001	20.7%	22.7%	0.359
Melanoma		(n=925)	(n=878)		(n=1,119)	(n=688)	
	Yes	2.5%	3.1%	0.537	2.7%	2.9%	0.891
Skin or Systemic Neoplasm		(n=994)	(n=918)		(n=1,192)	(n=724)	
	Yes	64.1%	62.9%	0.610	62.9%	64.5%	0.516
Malignant Skin or Systemic Neoplasm		(n=996)	(n=921)		(n=1,196)	(n=725)	
	Yes	31.5%	26.5%	0.018	28.4%	30.2%	0.435

Dependent Variable	Level	Cumulative Herbicide Exposure		
		Yes	No	p-Value
Any Systemic Neoplasm		(n=1,264)	(n=671)	
	Yes	34.7%	31.7%	0.216
Malignant Systemic Neoplasm		(n=1,270)	(n=671)	
	Yes	11.7%	9.8%	0.234
Benign Systemic Neoplasm		(n=1,264)	(n=671)	
	Yes	25.8%	23.9%	0.377
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature		(n=1,270)	(n=671)	
	Yes	2.3%	1.6%	0.434
Malignant Systemic Neoplasm of the Eye, Ear, Face, Head, or Neck		(n=1,270)	(n=671)	
	Yes	0.2%	0.3%	0.999
Malignant Systemic Neoplasm of the Oral Cavity, Pharynx, or Larynx		(n=1,270)	(n=671)	
	Yes	0.6%	0.8%	0.997
Malignant Systemic Neoplasm of the Thymus or Mediastinum		(n=1,270)	(n=671)	
	Yes	0.2%	0.2%	0.999
Malignant Systemic Neoplasm of the Thyroid Gland		(n=1,270)	(n=671)	
	Yes	0.2%	0.2%	0.999
Malignant Systemic Neoplasm of the Bronchus or Lung		(n=1,270)	(n=671)	
	Yes	1.4%	0.3%	0.037
Any Systemic Neoplasm of the Stomach		(n=1,270)	(n=671)	
	Yes	0.9%	0.5%	0.450
Malignant Systemic Neoplasm of the Colon or Rectum		(n=1,270)	(n=671)	
	Yes	1.3%	0.9%	0.618
Malignant Systemic Neoplasm of the Urinary System		(n=1,270)	(n=671)	
	Yes	1.7%	1.2%	0.469
Malignant Systemic Neoplasm of the Kidney or Ureter		(n=1,270)	(n=671)	
	Yes	0.6%	0.5%	0.847
Malignant Systemic Neoplasm of the Prostate		(n=1,270)	(n=671)	
	Yes	6.4%	5.8%	0.694
Malignant Systemic Neoplasm of the Penis or Other Male Genital Organs		(n=1,270)	(n=671)	
	Yes	0.2%	0.0%	0.776
Malignant Systemic Neoplasm of the Testicles		(n=1,270)	(n=671)	
	Yes	0.2%	0.0%	0.514
Malignant Systemic Neoplasm of Bone or Articular Cartilage		(n=1,270)	(n=671)	
	Yes	0.1%	0.5%	0.240
Malignant Systemic Neoplasm of Connective or Other Soft Tissues		(n=1,270)	(n=671)	
	Yes	0.4%	0.3%	0.999
Carcinoma in Situ		(n=1,270)	(n=671)	
	Yes	0.3%	0.9%	0.173
Hodgkin's Disease		(n=1,270)	(n=671)	
	Yes	0.2%	0.0%	0.776

Table F-2. Dependent Variable-covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Cumulative Herbicide Exposure		
		Yes	No	p-Value
Leukemia		(n=1,270)	(n=671)	
	Yes	0.5%	0.6%	0.977
Other Malignant Systemic Neoplasms of Lymphoid or Histiocytic Tissue		(n=1,270)	(n=671)	
	Yes	0.9%	0.5%	0.358
Lymphoreticular Sarcoma		(n=1,270)	(n=671)	
	Yes	0.2%	0.3%	0.902
Skin or Systemic Neoplasm		(n=1,249)	(n=667)	
	Yes	66.1%	58.8%	0.002
Malignant Skin or Systemic Neoplasm		(n=1,254)	(n=667)	
	Yes	31.3%	24.9%	0.004
PSA (ng/mL)		(n=1,180)	(n=623)	
(continuous)[a]	--	O = 0.95	O = 0.99	0.350
(discrete)	High	4.4%	6.1%	0.145

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	>0-10	>10	p-Value
Any Systemic Neoplasm		(n=595)	(n=488)	(n=849)	
	Yes	32.4%	33.4%	34.8%	0.650
Malignant Systemic Neoplasm		(n=596)	(n=489)	(n=853)	
	Yes	10.1%	8.4%	13.4%	0.013
Benign Systemic Neoplasm		(n=595)	(n=488)	(n=849)	
	Yes	24.2%	26.4%	25.1%	0.700
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature		(n=596)	(n=489)	(n=853)	
	Yes	2.0%	1.4%	2.5%	0.440
Malignant Systemic Neoplasm of the Eye, Ear, Face, Head, or Neck		(n=596)	(n=489)	(n=853)	
	Yes	0.2%	0.0%	0.5%	0.231
Malignant Systemic Neoplasm of the Oral Cavity, Pharynx, or Larynx		(n=596)	(n=489)	(n=853)	
	Yes	0.3%	0.6%	0.9%	0.379
Malignant Systemic Neoplasm of the Thymus or Mediastinum		(n=596)	(n=489)	(n=853)	
	Yes	0.0%	0.0%	0.4%	0.148
Malignant Systemic Neoplasm of the Thyroid Gland		(n=596)	(n=489)	(n=853)	
	Yes	0.3%	0.0%	0.1%	0.351
Malignant Systemic Neoplasm of the Bronchus or Lung		(n=596)	(n=489)	(n=853)	
	Yes	0.2%	0.2%	2.1%	<0.001
Any Systemic Neoplasm of the Stomach		(n=596)	(n=489)	(n=853)	
	Yes	0.8%	0.2%	0.9%	0.287
Malignant Systemic Neoplasm of the Colon or Rectum		(n=596)	(n=489)	(n=853)	
	Yes	0.5%	0.8%	1.8%	0.064
Malignant Systemic Neoplasm of the Urinary System		(n=596)	(n=489)	(n=853)	
	Yes	0.8%	1.4%	2.1%	0.151

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	>0-10	>10	p-Value
Malignant Systemic Neoplasm of the Kidney or Ureter		(n=596)	(n=489)	(n=853)	
	Yes	0.3%	0.2%	0.9%	0.151
Malignant Systemic Neoplasm of the Prostate		(n=596)	(n=489)	(n=853)	
	Yes	6.9%	4.5%	6.7%	0.197
Malignant Systemic Neoplasm of the Penis or Other Male Genital Organs		(n=596)	(n=489)	(n=853)	
	Yes	0.2%	0.0%	0.1%	0.683
Malignant Systemic Neoplasm of the Testicles		(n=596)	(n=489)	(n=853)	
	Yes	0.0%	0.2%	0.2%	0.509
Malignant Systemic Neoplasm of Bone or Articular Cartilage		(n=596)	(n=489)	(n=853)	
	Yes	0.2%	0.0%	0.4%	0.381
Malignant Systemic Neoplasm of Connective or Other Soft Tissues		(n=596)	(n=489)	(n=853)	
	Yes	0.2%	0.2%	0.6%	0.341
Carcinoma in Situ		(n=596)	(n=489)	(n=853)	
	Yes	0.3%	0.6%	0.6%	0.759
Hodgkin's Disease		(n=596)	(n=489)	(n=853)	
	Yes	0.2%	0.0%	0.1%	0.683
Leukemia		(n=596)	(n=489)	(n=853)	
	Yes	0.5%	0.4%	0.6%	0.908
Other Malignant Systemic Neoplasms of Lymphoid or Histiocytic Tissue		(n=596)	(n=489)	(n=853)	
	Yes	0.5%	0.2%	1.3%	0.061
Lymphoreticular Sarcoma		(n=596)	(n=489)	(n=853)	
	Yes	0.3%	0.2%	0.1%	0.666
Skin or Systemic Neoplasm		(n=590)	(n=481)	(n=842)	
	Yes	63.1%	62.4%	64.5%	0.715
Malignant Skin or Systemic Neoplasm		(n=591)	(n=482)	(n=845)	
	Yes	28.4%	24.1%	32.3%	0.006
PSA (ng/mL)		(n=554)	(n=456)	(n=790)	
(continuous)[a]	--		r = -0.020		0.398
(discrete)	High	5.2%	5.9%	4.3%	0.431

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	>0-40	>40	p-Value
Any Systemic Neoplasm		(n=106)	(n=1,226)	(n=595)	
	Yes	32.1%	33.9%	33.5%	0.928
Malignant Systemic Neoplasm		(n=107)	(n=1,228)	(n=597)	
	Yes	12.2%	11.3%	10.4%	0.783
Benign Systemic Neoplasm		(n=106)	(n=1,226)	(n=595)	
	Yes	22.6%	25.0%	25.9%	0.761
Systemic Neoplasm of Uncertain Behavior or Unspecified Nature		(n=107)	(n=1,228)	(n=597)	
	Yes	0.9%	1.8%	2.9%	0.231
Malignant Systemic Neoplasm of the Eye, Ear, Face, Head, or Neck		(n=107)	(n=1,228)	(n=597)	
	Yes	0.9%	0.3%	0.0%	0.161

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			p-Value
		0	**>0-40**	**>40**	
Malignant Systemic Neoplasm of the Oral Cavity, Pharynx, or Larynx	Yes	(n=107) 0.0%	(n=1,228) 0.8%	(n=597) 0.5%	0.509
Malignant Systemic Neoplasm of the Thymus or Mediastinum	Yes	(n=107) 0.0%	(n=1,228) 0.2%	(n=597) 0.2%	0.915
Malignant Systemic Neoplasm of the Thyroid Gland	Yes	(n=107) 0.0%	(n=1,228) 0.2%	(n=597) 0.2%	0.915
Malignant Systemic Neoplasm of the Bronchus or Lung	Yes	(n=107) 0.0%	(n=1,228) 1.0%	(n=597) 1.3%	0.427
Any Systemic Neoplasm of the Stomach	Yes	(n=107) 1.9%	(n=1,228) 0.6%	(n=597) 0.8%	0.292
Malignant Systemic Neoplasm of the Colon or Rectum	Yes	(n=107) 0.0%	(n=1,228) 1.0%	(n=597) 1.7%	0.218
Malignant Systemic Neoplasm of the Urinary System	Yes	(n=107) 4.7%	(n=1,228) 1.4%	(n=597) 1.2%	0.020
Malignant Systemic Neoplasm of the Kidney or Ureter	Yes	(n=107) 1.9%	(n=1,228) 0.5%	(n=597) 0.3%	0.122
Malignant Systemic Neoplasm of the Prostate	Yes	(n=107) 5.6%	(n=1,228) 6.4%	(n=597) 5.9%	0.893
Malignant Systemic Neoplasm of the Penis or Other Male Genital Organs	Yes	(n=107) 0.9%	(n=1,228) 0.1%	(n=597) 0.0%	0.020
Malignant Systemic Neoplasm of the Testicles	Yes	(n=107) 0.0%	(n=1,228) 0.2%	(n=597) 0.0%	0.423
Malignant Systemic Neoplasm of Bone or Articular Cartilage	Yes	(n=107) 0.0%	(n=1,228) 0.2%	(n=597) 0.3%	0.667
Malignant Systemic Neoplasm of Connective or Other Soft Tissues	Yes	(n=107) 0.9%	(n=1,228) 0.4%	(n=597) 0.2%	0.435
Carcinoma in Situ	Yes	(n=107) 0.0%	(n=1,228) 0.6%	(n=597) 0.5%	0.732
Hodgkin's Disease	Yes	(n=107) 0.0%	(n=1,228) 0.2%	(n=597) 0.0%	0.563
Leukemia	Yes	(n=107) 0.0%	(n=1,228) 0.6%	(n=597) 0.5%	0.732
Other Malignant Systemic Neoplasms of Lymphoid or Histiocytic Tissue	Yes	(n=107) 0.0%	(n=1,228) 0.9%	(n=597) 0.7%	0.562
Lymphoreticular Sarcoma	Yes	(n=107) 0.0%	(n=1,228) 0.2%	(n=597) 0.2%	0.840
Skin or Systemic Neoplasm	Yes	(n=103) 70.9%	(n=1,215) 63.3%	(n=590) 62.7%	0.273
Malignant Skin or Systemic Neoplasm	Yes	(n=104) 29.8%	(n=1,217) 29.0%	(n=591) 28.9%	0.983

Table F-2. Dependent Variable-covariate Associations for the Neoplasia Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			p-Value
		0	**>0-40**	**>40**	
PSA (ng/mL)		(n=98)	(n=1,140)	(n=557)	
(continuous)[a]	--		r = -0.018		0.448
(discrete)	High	6.1%	4.6%	5.8%	0.505

[a]Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.

--: The covariate was not applicable for this dependent variable.

Note: Correlations (r) are based on total sample size and are not category-specific.

Please see Section 10.1.3 and Table 10-1 for a further discussion of the dependent variables and covariates shown in this appendix.

Table F-3. Dependent Variable-covariate Associations for the Neurology Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Inflammatory Diseases		(n=881)	(n=1,054)		(n=122)	(n=1,813)	
	Yes	0.8%	0.9%	0.999	0.8%	0.8%	0.999
Hereditary and Degenerative Diseases	Yes	(n=885)	(n=1,058)		(n=122)	(n=1,821)	
		11.9%	17.6%	<0.001	9.8%	15.3%	0.130
Peripheral Disorders		(n=884)	(n=1,053)		(n=122)	(n=1,815)	
	Yes	20.5%	31.8%	<0.001	21.3%	27.0%	0.204
Other Neurological Disorders	Yes	(n=882)	(n=1,056)		(n=122)	(n=1,816)	
		13.7%	21.7%	<0.001	32.0%	17.1%	<0.001
Smell		(n=884)	(n=1,057)		(n=122)	(n=1,819)	
	Abnormal	1.9%	2.9%	0.201	2.5%	2.5%	0.999
Visual Fields		(n=880)	(n=1,046)		(n=120)	(n=1,806)	
	Abnormal	0.6%	1.3%	0.141	0.0%	1.1%	0.514
Light Reaction		(n=883)	(n=1,054)		(n=120)	(n=1,817)	
	Abnormal	0.6%	0.7%	0.999	0.0%	0.7%	0.770
Ocular Movement		(n=884)	(n=1,054)		(n=121)	(n=1,817)	
	Abnormal	0.5%	0.5%	0.999	0.0%	0.5%	0.932
Facial Sensation		(n=885)	(n=1,057)		(n=122)	(n=1,820)	
	Abnormal	0.2%	0.5%	0.600	0.8%	0.3%	0.925
Corneal Reflex		(n=880)	(n=1,054)		(n=121)	(n=1,813)	
	Abnormal	0.3%	0.4%	0.999	0.0%	0.4%	0.999
Smile		(n=885)	(n=1,057)		(n=122)	(n=1,820)	
	Abnormal	0.8%	1.1%	0.592	0.0%	1.0%	0.510
Palpebral Fissure		(n=885)	(n=1,056)		(n=122)	(n=1,819)	
	Abnormal	1.8%	2.8%	0.180	3.3%	2.3%	0.708
Balance		(n=884)	(n=1,056)		(n=121)	(n=1,819)	
	Abnormal	0.7%	3.2%	<0.001	0.0%	2.2%	0.188
Gag Reflex		(n=885)	(n=1,057)		(n=122)	(n=1,820)	
	Abnormal	0.2%	0.1%	0.878	0.0%	0.2%	0.999
Speech		(n=885)	(n=1,057)		(n=122)	(n=1,820)	
	Abnormal	0.6%	1.6%	0.051	0.0%	1.2%	0.436
Tongue Position Relative to Midline	Deviated	(n=885)	(n=1,057)		(n=122)	(n=1,820)	
		0.1%	0.4%	0.484	0.0%	0.3%	0.999
Shoulder Shrug		(n=885)	(n=1,057)		(n=122)	(n=1,820)	
	Abnormal	0.6%	0.4%	0.789	0.8%	0.4%	0.999
Cranial Nerve Index		(n=876)	(n=1,049)		(n=120)	(n=1805)	
	Abnormal	6.4%	11.0%	<0.001	6.7%	9.0%	0.474
Pinprick		(n=778)	(n=843)		(n=104)	(n=1,517)	
	Abnormal	6.3%	12.8%	<0.001	12.5%	9.5%	0.406
Light Touch		(n=778)	(n=843)		(n=104)	(n=1,517)	
	Abnormal	3.6%	8.1%	<0.001	5.8%	5.9%	0.999

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Muscle Status		(n=882)	(n=1,054)		(n=121)	(n=1,815)	
	Abnormal	4.3%	6.0%	0.123	4.1%	5.3%	0.732
Patellar Reflex		(n=882)	(n=1,052)		(n=120)	(n=1,814)	
	Absent	3.4%	3.6%	<0.001	5.8%	3.4%	0.056
	Sluggish	17.5%	26.9%		29.2%	22.2%	
	Active or Very Active	79.1%	69.5%		65.0%	74.5%	
Achilles Reflex		(n=882)	(n=1,055)		(n=121)	(n=1,816)	
	Absent	13.8%	30.2%	<0.001	30.6%	22.3%	0.079
	Sluggish	32.3%	37.8%		34.7%	35.4%	
	Active or Very Active	53.9%	31.9%		34.7%	42.4%	
Biceps Reflex		(n=885)	(n=1,056)		(n=122)	(n=1,819)	
	Absent	1.6%	2.7%	<0.001	4.1%	2.0%	0.208
	Sluggish	23.1%	30.9%		30.3%	27.1%	
	Active or Very Active	75.4%	66.5%		65.6%	70.9%	
Babinski Reflex		(n=884)	(n=1,053)		(n=121)	(n=1,816)	
	Abnormal	1.7%	1.2%	0.511	4.1%	1.3%	0.031
Any Symmetrical Peripheral Abnormality	Abnormal	(n=861) 13.9%	(n=1,019) 30.8%	<0.001	(n=118) 28.8%	(n=1,762) 22.7%	0.158
Possible Peripheral Neuropathy	Abnormal	(n=861) 13.2%	(n=1,020) 29.7%	<0.001	(n=118) 28.0%	(n=1,763) 21.8%	0.147
Probable Peripheral Neuropathy	Abnormal	(n=861) 2.8%	(n=1,019) 11.5%	<0.001	(n=118) 9.3%	(n=1,762) 7.4%	0.551
Tremor		(n=885)	(n=1,057)		(n=122)	(n=1,820)	
	Abnormal	6.0%	8.2%	0.070	5.7%	7.3%	0.640
Coordination		(n=884)	(n=1,054)		(n=120)	(n=1,818)	
	Abnormal	2.2%	6.9%	<0.001	3.3%	4.8%	0.596
Romberg Sign		(n=884)	(n=1,056)		(n=121)	(n=1,819)	
	Abnormal	0.7%	3.2%	<0.001	0.0%	2.2%	0.188
Gait		(n=885)	(n=1,057)		(n=122)	(n=1,820)	
	Abnormal	4.5%	11.6%	<0.001	6.6%	8.5%	0.557
CNS Index		(n=885)	(n=1,057)		(n=122)	(n=1,820)	
	Abnormal	10.4%	19.3%	<0.001	12.3%	15.4%	0.421

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Inflammatory Diseases		(n=764)	(n=314)	(n=857)	
	Yes	0.5%	1.0%	1.1%	0.486
Hereditary and Degenerative Diseases		(n=768)	(n=316)	(n=859)	
	Yes	14.8%	17.4%	14.2%	0.391

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Peripheral Disorders		(n=765)	(n=314)	(n=858)	
	Yes	27.1%	28.7%	25.5%	0.529
Other Neurological Disorders		(n=766)	(n=315)	(n=857)	
	Yes	8.4%	27.6%	23.2%	<0.001
Smell		(n=767)	(n=315)	(n=859)	
	Abnormal	2.7%	2.5%	2.2%	0.790
Visual Fields		(n=762)	(n=314)	(n=850)	
	Abnormal	1.1%	1.3%	0.8%	0.768
Light Reaction		(n=767)	(n=314)	(n=856)	
	Abnormal	0.4%	0.0%	1.1%	0.074
Ocular Movement		(n=767)	(n=314)	(n=857)	
	Abnormal	0.5%	0.3%	0.5%	0.905
Facial Sensation		(n=767)	(n=316)	(n=859)	
	Abnormal	0.3%	1.0%	0.2%	0.161
Corneal Reflex		(n=767)	(n=314)	(n=853)	
	Abnormal	0.4%	0.3%	0.4%	0.982
Smile		(n=767)	(n=316)	(n=859)	
	Abnormal	1.3%	1.0%	0.7%	0.464
Palpebral Fissure		(n=767)	(n=316)	(n=858)	
	Abnormal	2.5%	3.5%	1.9%	0.263
Balance		(n=767)	(n=316)	(n=857)	
	Abnormal	2.5%	3.2%	1.3%	0.077
Gag Reflex		(n=767)	(n=316)	(n=859)	
	Abnormal	0.0%	0.6%	0.1%	0.051
Speech		(n=767)	(n=316)	(n=859)	
	Abnormal	1.0%	0.6%	1.4%	0.523
Tongue Position Relative to Midline		(n=767)	(n=316)	(n=859)	
	Deviated	0.3%	0.6%	0.1%	0.301
Shoulder Shrug		(n=767)	(n=316)	(n=859)	
	Abnormal	0.5%	0.6%	0.4%	0.781
Cranial Nerve Index		(n=763)	(n=315)	(n=847)	
	Abnormal	9.3%	9.8%	8.2%	0.579
Pinprick		(n=648)	(n=256)	(n=717)	
	Abnormal	9.0%	13.3%	9.1%	0.105
Light Touch		(n=648)	(n=256)	(n=717)	
	Abnormal	5.1%	8.2%	5.9%	0.202
Muscle Status		(n=764)	(n=316)	(n=856)	
	Abnormal	5.0%	6.3%	5.0%	0.623
Patellar Reflex		(n=764)	(n=316)	(n=854)	
	Absent	3.9%	2.9%	3.4%	0.634
	Sluggish	23.2%	24.7%	21.3%	
	Active or Very Active	72.9%	72.5%	75.3%	

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Achilles Reflex		(n=765)	(n=315)	(n=857)	
	Absent	24.7%	27.0%	19.5%	0.002
	Sluggish	36.0%	37.1%	34.1%	
	Active or Very Active	39.4%	35.9%	46.4%	
Biceps Reflex		(n=767)	(n=316)	(n=858)	
	Absent	1.8%	3.8%	1.9%	0.274
	Sluggish	27.4%	28.2%	26.9%	
	Active or Very Active	70.8%	68.0%	71.2%	
Babinski Reflex		(n=765)	(n=316)	(n=856)	
	Abnormal	0.9%	2.5%	1.5%	0.125
Any Symmetrical Peripheral Abnormality		(n=743)	(n=306)	(n=831)	
	Abnormal	24.0%	27.1%	20.8%	0.063
Possible Peripheral Neuropathy		(n=743)	(n=307)	(n=831)	
	Abnormal	23.0%	25.7%	20.1%	0.098
Probable Peripheral Neuropathy		(n=743)	(n=307)	(n=830)	
	Abnormal	8.6%	9.1%	5.9%	0.063
Tremor		(n=767)	(n=316)	(n=859)	
	Abnormal	6.8%	7.6%	7.5%	0.837
Coordination		(n=767)	(n=315)	(n=856)	
	Abnormal	4.2%	6.0%	4.8%	0.425
Romberg Sign		(n=767)	(n=316)	(n=857)	
	Abnormal	2.5%	3.2%	1.3%	0.077
Gait		(n=767)	(n=316)	(n=859)	
	Abnormal	8.2%	10.1%	7.9%	0.467
CNS Index		(n=767)	(n=316)	(n=859)	
	Abnormal	14.2%	17.4%	15.4%	0.410

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	>0-40	>40	p-Value
Inflammatory Diseases		(n=106)	(n=1,224)	(n=596)	
	Yes	0.0%	0.7%	1.3%	0.197
Hereditary and Degenerative Diseases		(n=107)	(n=1,229)	(n=598)	
	Yes	13.1%	14.5%	16.2%	0.532
Peripheral Disorders		(n=107)	(n=1,225)	(n=596)	
	Yes	29.9%	25.7%	27.7%	0.484
Other Neurological Disorders		(n=106)	(n=1,226)	(n=597)	
	Yes	22.6%	17.8%	17.6%	0.437
Smell		(n=107)	(n=1,228)	(n=597)	
	Abnormal	3.7%	2.4%	2.5%	0.680
Visual Fields		(n=105)	(n=1,221)	(n=591)	
	Abnormal	0.0%	1.0%	1.0%	0.589

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	>0-40	>40	p-Value
Light Reaction		(n=107)	(n=1,225)	(n=596)	
	Abnormal	0.0%	0.5%	1.0%	0.295
Ocular Movement		(n=107)	(n=1,226)	(n=596)	
	Abnormal	0.9%	0.4%	0.5%	0.736
Facial Sensation		(n=107)	(n=1,228)	(n=598)	
	Abnormal	0.9%	0.2%	0.3%	0.465
Corneal Reflex		(n=107)	(n=1,223)	(n=595)	
	Abnormal	0.0%	0.4%	0.3%	0.790
Smile		(n=107)	(n=1,228)	(n=598)	
	Abnormal	0.0%	0.9%	1.0%	0.589
Palpebral Fissure		(n=107)	(n=1,227)	(n=598)	
	Abnormal	2.8%	2.0%	2.8%	0.533
Balance		(n=107)	(n=1,227)	(n=597)	
	Abnormal	4.7%	1.8%	2.2%	0.131
Gag Reflex		(n=107)	(n=1,228)	(n=598)	
	Abnormal	0.0%	0.2%	0.2%	0.916
Speech		(n=107)	(n=1,228)	(n=598)	
	Abnormal	1.9%	1.1%	0.7%	0.440
Tongue Position Relative to Midline	Deviated	(n=107)	(n=1,228)	(n=598)	
		0.0%	0.2%	0.3%	0.810
Shoulder Shrug		(n=107)	(n=1,228)	(n=598)	
	Abnormal	0.0%	0.5%	0.3%	0.704
Cranial Nerve Index		(n=105)	(n=1,219)	(n=592)	
	Abnormal	12.4%	8.0%	9.8%	0.194
Pinprick		(n=82)	(n=1,035)	(n=498)	
	Abnormal	9.8%	9.7%	9.4%	0.989
Light Touch		(n=82)	(n=1,035)	(n=498)	
	Abnormal	3.7%	6.2%	5.6%	0.618
Muscle Status		(n=107)	(n=1225)	(n=595)	
	Abnormal	8.4%	4.9%	5.0%	0.285
Patellar Reflex		(n=107)	(n=1,223)	(n=596)	
	Absent	8.4%	3.1%	3.5%	0.017
	Sluggish	22.4%	21.2%	25.2%	
	Active or Very Active	69.2%	75.7%	71.3%	
Achilles Reflex		(n=106)	(n=1,224)	(n=598)	
	Absent	26.4%	20.1%	27.4%	<0.001
	Sluggish	24.5%	36.3%	35.1%	
	Active or Very Active	49.1%	43.6%	37.5%	
Biceps Reflex		(n=107)	(n=1,228)	(n=597)	
	Absent	3.7%	1.6%	3.2%	<0.001
	Sluggish	30.8%	24.4%	32.5%	
	Active or Very Active	65.4%	74.0%	64.3%	

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	**>0-40**	**>40**	**p-Value**
Babinski Reflex		(n=107)	(n=1,224)	(n=597)	
	Abnormal	0.9%	1.8%	0.8%	0.247
Any Symmetrical Peripheral Abnormality		(n=104)	(n=1,204)	(n=563)	
	Abnormal	26.0%	21.0%	26.6%	0.025
Possible Peripheral Neuropathy		(n=105)	(n=1,204)	(n=563)	
	Abnormal	25.7%	20.0%	25.8%	0.017
Probable Peripheral Neuropathy		(n=104)	(n=1,204)	(n=563)	
	Abnormal	9.6%	7.4%	6.9%	0.628
Tremor		(n=107)	(n=1,228)	(n=598)	
	Abnormal	9.4%	6.5%	8.4%	0.248
Coordination		(n=107)	(n=1,226)	(n=597)	
	Abnormal	10.3%	4.2%	4.9%	0.016
Romberg Sign		(n=107)	(n=1,227)	(n=597)	
	Abnormal	4.7%	1.8%	2.2%	0.131
Gait		(n=107)	(n=1,228)	(n=598)	
	Abnormal	11.2%	7.2%	9.9%	0.073
CNS Index		(n=107)	(n=1,228)	(n=598)	
	Abnormal	21.5%	13.5%	17.2%	0.019

Dependent Variable	Level	Body Mass Index (kg/m^2)			Cumulative Insecticide Exposure		
		Not Obese (≤30)	**Obese (>30)**	**p-Value**	**Yes**	**No**	**p-Value**
Inflammatory Diseases		(n=1,249)	(n=685)		(n=1,409)	(n=526)	
	Yes	0.8%	0.9%	0.999	0.6%	1.3%	0.225
Hereditary and Degenerative Diseases		(n=1,255)	(n=687)		(n=1,415)	(n=528)	
	Yes	15.5%	14.1%	0.469	15.8%	12.9%	0.131
Peripheral Disorders		(n=1,250)	(n=686)		(n=1,409)	(n=528)	
	Yes	24.7%	30.2%	0.011	27.4%	24.6%	0.241
Other Neurological Disorders		(n=1,252)	(n=685)		(n=1,411)	(n=527)	
	Yes	18.0%	18.3%	0.929	19.6%	14.0%	0.006
Smell		(n=1,254)	(n=687)		(n=1,413)	(n=528)	
	Abnormal	2.5%	2.5%	0.999	2.3%	2.8%	0.636
Visual Fields		(n=1,243)	(n=683)		(n=1,405)	(n=521)	
	Abnormal	0.9%	1.2%	0.713	1.1%	0.8%	0.740
Light Reaction		(n=1,251)	(n=686)		(n=1,411)	(n=526)	
	Abnormal	0.7%	0.4%	0.650	0.6%	0.6%	0.999
Ocular Movement		(n=1,252)	(n=686)		(n=1,411)	(n=527)	
	Abnormal	0.6%	0.3%	0.632	0.4%	0.8%	0.429
Facial Sensation		(n=1,255)	(n=687)		(n=1,414)	(n=528)	
	Abnormal	0.5%	0.2%	0.439	0.4%	0.2%	0.732
Corneal Reflex		(n=1,251)	(n=683)		(n=1,408)	(n=526)	
	Abnormal	0.5%	0.2%	0.441	0.4%	0.4%	0.999

Table F-3. Dependent Variable-covariate Associations for the Neurology Assessment (Continued)

Dependent Variable	Level	Body Mass Index (kg/m^2) Not Obese (≤30)	Obese (>30)	p-Value	Cumulative Insecticide Exposure Yes	No	p-Value
Smile		(n=1,255)	(n=687)		(n=1,414)	(n=528)	
	Abnormal	0.7%	1.5%	0.180	1.2%	0.4%	0.167
Palpebral Fissure		(n=1,255)	(n=686)		(n=1,413)	(n=528)	
	Abnormal	2.4%	2.3%	0.999	2.6%	1.9%	0.500
Balance		(n=1,253)	(n=687)		(n=1,412)	(n=528)	
	Abnormal	2.0%	2.2%	0.911	2.1%	1.9%	0.890
Gag Reflex		(n=1,255)	(n=687)		(n=1,414)	(n=528)	
	Abnormal	0.2%	0.0%	0.498	0.2%	0.0%	0.682
Speech		(n=1,255)	(n=687)		(n=1,414)	(n=528)	
	Abnormal	1.2%	1.0%	0.899	1.0%	1.5%	0.464
Tongue Position Relative to Midline	Deviated	(n=1,255) 0.2%	(n=687) 0.3%	0.999	(n=1,414) 0.3%	(n=528) 0.2%	0.999
Shoulder Shrug		(n=1,255)	(n=687)		(n=1,414)	(n=528)	
	Abnormal	0.3%	0.7%	0.358	0.6%	0.0%	0.144
Cranial Nerve Index		(n=1,244)	(n=681)		(n=1,403)	(n=522)	
	Abnormal	8.8%	9.0%	0.999	9.0%	8.6%	0.875
Pinprick		(n=1,138)	(n=483)		(n=1,173)	(n=448)	
	Abnormal	9.4%	10.4%	0.618	10.4%	7.8%	0.138
Light Touch		(n=1,138)	(n=483)		(n=1,173)	(n=448)	
	Abnormal	5.7%	6.4%	0.663	6.4%	4.7%	0.236
Muscle Status		(n=1,251)	(n=685)		(n=1,408)	(n=528)	
	Abnormal	5.6%	4.5%	0.365	5.9%	3.4%	0.038
Patellar Reflex		(n=1,249)	(n=685)		(n=1,410)	(n=524)	
	Absent	2.8%	4.8%	<0.001	3.4%	3.8%	0.694
	Sluggish	20.6%	26.3%		22.2%	23.7%	
	Active or Very Active	76.6%	68.9%		74.4%	72.5%	
Achilles Reflex		(n=1,251)	(n=686)		(n=1,411)	(n=526)	
	Absent	20.5%	27.0%	<0.001	23.0%	22.1%	0.262
	Sluggish	34.8%	36.3%		36.1%	33.1%	
	Active or Very Active	44.8%	36.7%		40.8%	44.9%	
Biceps Reflex		(n=1,254)	(n=687)		(n=1,413)	(n=528)	
	Absent	2.0%	2.5%	0.063	2.2%	2.1%	0.237
	Sluggish	25.7%	30.3%		26.3%	30.1%	
	Active or Very Active	72.3%	67.3%		71.6%	67.8%	
Babinski Reflex		(n=1,250)	(n=687)		(n=1,410)	(n=527)	
	Abnormal	0.8%	2.6%	0.003	1.4%	1.5%	0.999
Any Symmetrical Peripheral Abnormality	Abnormal	(n=1,208) 20.3%	(n=672) 28.1%	<0.001	(n=1,369) 24.0%	(n=511) 20.7%	0.158
Possible Peripheral Neuropathy	Abnormal	(n=1,208) 19.4%	(n=673) 27.2%	<0.001	(n=1,370) 22.8%	(n=511) 20.6%	0.331

Table F-3. Dependent Variable-covariate Associations for the Neurology Assessment (Continued)

Dependent Variable	Level	Body Mass Index (kg/m^2)			Cumulative Insecticide Exposure		
		Not Obese (≤30)	Obese (>30)	p-Value	Yes	No	p-Value
Probable Peripheral Neuropathy	Abnormal	(n=1,207) 6.6%	(n=673) 9.2%	0.044	(n=1,369) 7.7%	(n=511) 7.1%	0.720
Tremor	Abnormal	(n=1,255) 7.0%	(n=687) 7.6%	0.717	(n=1,414) 7.4%	(n=528) 6.6%	0.613
Coordination	Abnormal	(n=1,253) 4.5%	(n=685) 5.3%	0.505	(n=1,410) 4.7%	(n=528) 4.9%	0.917
Romberg Sign	Abnormal	(n=1,253) 2.0%	(n=687) 2.2%	0.911	(n=1,412) 2.1%	(n=528) 1.9%	0.890
Gait	Abnormal	(n=1,255) 7.9%	(n=687) 9.3%	0.318	(n=1,414) 8.6%	(n=528) 7.8%	0.604
CNS Index	Abnormal	(n=1,255) 14.6%	(n=687) 16.5%	0.304	(n=1,414) 16.0%	(n=528) 13.3%	0.157

Dependent Variable	Level	Cumulative Degreasing Chemical Exposure			Cumulative Industrial Chemical Exposure		
		Yes	No	p-Value	Yes	No	p-Value
Inflammatory Diseases	Yes	(n=1,248) 1.0%	(n=687) 0.4%	0.253	(n=1,211) 1.1%	(n=724) 0.4%	0.197
Hereditary and Degenerative Diseases	Yes	(n=1,254) 14.7%	(n=689) 15.5%	0.660	(n=1,215) 15.8%	(n=728) 13.6%	0.211
Peripheral Disorders	Yes	(n=1,248) 27.8%	(n=689) 24.5%	0.132	(n=1,211) 26.4%	(n=726) 27.0%	0.824
Other Neurological Disorders	Yes	(n=1,251) 20.1%	(n=687) 14.3%	0.002	(n=1,211) 20.5%	(n=727) 14.0%	<0.001
Smell	Abnormal	(n=1,253) 2.1%	(n=688) 3.2%	0.171	(n=1,214) 2.5%	(n=727) 2.5%	0.999
Visual Fields	Abnormal	(n=1,245) 1.2%	(n=681) 0.6%	0.285	(n=1,203) 1.2%	(n=723) 0.7%	0.437
Light Reaction	Abnormal	(n=1,250) 0.8%	(n=687) 0.3%	0.288	(n=1,212) 0.7%	(n=725) 0.4%	0.553
Ocular Movement	Abnormal	(n=1,250) 0.6%	(n=688) 0.3%	0.628	(n=1,213) 0.6%	(n=725) 0.3%	0.550
Facial Sensation	Abnormal	(n=1,254) 0.3%	(n=688) 0.4%	0.987	(n=1,215) 0.4%	(n=727) 0.3%	0.925
Corneal Reflex	Abnormal	(n=1,246) 0.5%	(n=688) 0.2%	0.434	(n=1,210) 0.3%	(n=724) 0.4%	0.999
Smile	Abnormal	(n=1,254) 1.2%	(n=688) 0.6%	0.282	(n=1,215) 1.2%	(n=727) 0.7%	0.442
Palpebral Fissure	Abnormal	(n=1,253) 2.6%	(n=688) 1.9%	0.382	(n=1,214) 2.4%	(n=727) 2.3%	0.999

Dependent Variable	Level	Cumulative Degreasing Chemical Exposure			Cumulative Industrial Chemical Exposure		
		Yes	No	p-Value	Yes	No	p-Value
Balance		(n=1,253)	(n=687)		(n=1,214)	(n=726)	
	Abnormal	2.1%	2.0%	0.999	1.9%	2.3%	0.613
Gag Reflex		(n=1,254)	(n=688)		(n=1,215)	(n=727)	
	Abnormal	0.2%	0.2%	0.999	0.2%	0.1%	0.999
Speech		(n=1,254)	(n=688)		(n=1,215)	(n=727)	
	Abnormal	1.0%	1.3%	0.752	1.0%	1.4%	0.575
Tongue Position Relative to Midline	Deviated	(n=1,254) 0.3%	(n=688) 0.2%	0.799	(n=1,215) 0.3%	(n=727) 0.3%	0.999
Shoulder Shrug		(n=1,254)	(n=688)		(n=1,215)	(n=727)	
	Abnormal	0.6%	0.2%	0.238	0.5%	0.4%	0.999
Cranial Nerve Index		(n=1,243)	(n=682)		(n=1,202)	(n=723)	
	Abnormal	9.3%	8.1%	0.395	9.2%	8.4%	0.652
Pinprick		(n=1,048)	(n=573)		(n=1,020)	(n=601)	
	Abnormal	9.8%	9.4%	0.861	9.6%	9.8%	0.960
Light Touch		(n=1,048)	(n=573)		(n=1,020)	(n=601)	
	Abnormal	6.1%	5.6%	0.752	5.5%	6.7%	0.395
Muscle Status		(n=1,251)	(n=685)		(n=1,212)	(n=724)	
	Abnormal	4.9%	5.8%	0.421	5.2%	5.3%	0.999
Patellar Reflex		(n=1,249)	(n=685)		(n=1,210)	(n=724)	
	Absent	3.1%	4.2%	0.364	3.4%	3.7%	0.845
	Sluggish	23.1%	21.6%		22.3%	23.1%	
	Active or Very Active	73.7%	74.2%		74.3%	73.2%	
Achilles Reflex		(n=1,252)	(n=685)		(n=1,213)	(n=724)	
	Absent	22.4%	23.5%	0.250	22.5%	23.2%	0.047
	Sluggish	34.4%	37.1%		33.6%	38.3%	
	Active or Very Active	43.3%	39.4%		43.9%	38.5%	
Biceps Reflex		(n=1,253)	(n=688)		(n=1,214)	(n=727)	
	Absent	2.5%	1.6%	0.438	2.6%	1.5%	0.296
	Sluggish	27.4%	27.2%		26.9%	27.9%	
	Active or Very Active	70.2%	71.2%		70.5%	70.6%	
Babinski Reflex		(n=1,252)	(n=685)		(n=1,212)	(n=725)	
	Abnormal	1.8%	0.9%	0.176	1.7%	1.1%	0.436
Any Symmetrical Peripheral Abnormality	Abnormal	(n=1,218) 23.1%	(n=662) 23.1%	0.999	(n=1,176) 23.2%	(n=704) 22.9%	0.908
Possible Peripheral Neuropathy	Abnormal	(n=1,218) 22.3%	(n=663) 22.0%	0.955	(n=1,177) 22.5%	(n=704) 21.6%	0.682
Probable Peripheral Neuropathy	Abnormal	(n=1,217) 7.4%	(n=663) 7.7%	0.887	(n=1,176) 7.5%	(n=704) 7.5%	0.999
Tremor		(n=1,254)	(n=688)		(n=1,215)	(n=727)	
	Abnormal	6.8%	8.0%	0.369	7.2%	7.2%	0.999

Dependent Variable	Level	Cumulative Degreasing Chemical Exposure			Cumulative Industrial Chemical Exposure		
		Yes	No	p-Value	Yes	No	p-Value
Coordination		(n=1,251)	(n=687)		(n=1,212)	(n=726)	
	Abnormal	4.6%	5.1%	0.674	4.6%	5.0%	0.819
Romberg Sign		(n=1,253)	(n=687)		(n=1,214)	(n=726)	
	Abnormal	2.1%	2.0%	0.999	1.9%	2.3%	0.613
Gait		(n=1,254)	(n=688)		(n=1,215)	(n=727)	
	Abnormal	7.9%	9.3%	0.325	7.6%	9.8%	0.109
CNS Index		(n=1,254)	(n=688)		(n=1,215)	(n=727)	
	Abnormal	14.8%	16.1%	0.457	14.7%	16.1%	0.458

Dependent Variable	Level	Diabetic Class			
		Normal	Impaired	Diabetic	p-Value
Inflammatory Diseases		(n=1,168)	(n=401)	(n=366)	
	Yes	0.8%	1.3%	0.6%	0.533
Hereditary and Degenerative Diseases		(n=1,173)	(n=402)	(n=368)	
	Yes	13.1%	15.4%	20.4%	0.003
Peripheral Disorders		(n=1,169)	(n=402)	(n=366)	
	Yes	21.1%	23.6%	47.5%	<0.001
Other Neurological Disorders		(n=1,168)	(n=402)	(n=368)	
	Yes	16.2%	18.7%	23.4%	0.007
Smell		(n=1,171)	(n=402)	(n=368)	
	Abnormal	2.2%	2.7%	3.0%	0.660
Visual Fields		(n=1,161)	(n=402)	(n=363)	
	Abnormal	0.9%	0.5%	1.9%	0.107
Light Reaction		(n=1,169)	(n=402)	(n=366)	
	Abnormal	0.6%	1.0%	0.3%	0.440
Ocular Movement		(n=1,170)	(n=402)	(n=366)	
	Abnormal	0.5%	0.5%	0.3%	0.836
Facial Sensation		(n=1,172)	(n=402)	(n=368)	
	Abnormal	0.4%	0.0%	0.5%	0.379
Corneal Reflex		(n=1,171)	(n=398)	(n=365)	
	Abnormal	0.3%	0.5%	0.6%	0.628
Smile		(n=1,172)	(n=402)	(n=368)	
	Abnormal	0.6%	0.0%	3.3%	<0.001
Palpebral Fissure		(n=1,171)	(n=402)	(n=368)	
	Abnormal	1.9%	2.7%	3.5%	0.165
Balance		(n=1,172)	(n=402)	(n=366)	
	Abnormal	1.0%	2.7%	4.6%	<0.001
Gag Reflex		(n=1,172)	(n=402)	(n=368)	
	Abnormal	0.1%	0.3%	0.3%	0.630
Speech		(n=1,172)	(n=402)	(n=368)	
	Abnormal	0.9%	1.5%	1.4%	0.598

Table F-3. Dependent Variable-covariate Associations for the Neurology Assessment (Continued)

Dependent Variable	Level	Diabetic Class			p-Value
		Normal	**Impaired**	**Diabetic**	
Tongue Position Relative to Midline	Deviated	(n=1,172) 0.3%	(n=402) 0.5%	(n=368) 0.0%	0.396
Shoulder Shrug	Abnormal	(n=1,172) 0.3%	(n=402) 0.5%	(n=368) 1.1%	0.122
Cranial Nerve Index	Abnormal	(n=1,164) 7.5%	(n=400) 11.0%	(n=361) 11.1%	0.027
Pinprick	Abnormal	(n=1,037) 5.5%	(n=319) 9.7%	(n=265) 26.0%	<0.001
Light Touch	Abnormal	(n=1,037) 3.2%	(n=319) 5.6%	(n=265) 17.0%	<0.001
Muscle Status	Abnormal	(n=1,170) 4.4%	(n=402) 4.5%	(n=364) 8.8%	0.003
Patellar Reflex	Absent	(n=1,166) 2.1%	(n=401) 3.2%	(n=367) 8.2%	<0.001
	Sluggish	19.1%	21.2%	35.2%	
	Active or Very Active	78.7%	75.6%	56.7%	
Achilles Reflex	Absent	(n=1,168) 15.8%	(n=401) 22.2%	(n=368) 45.7%	<0.001
	Sluggish	35.6%	36.9%	32.6%	
	Active or Very Active	48.6%	40.9%	21.7%	
Biceps Reflex	Absent	(n=1,171) 1.4%	(n=402) 1.5%	(n=368) 5.4%	<0.001
	Sluggish	23.7%	26.9%	39.1%	
	Active or Very Active	74.9%	71.6%	55.4%	
Babinski Reflex	Abnormal	(n=1,169) 1.3%	(n=402) 1.2%	(n=366) 2.2%	0.419
Any Symmetrical Peripheral Abnormality	Abnormal	(n=1,137) 15.5%	(n=390) 21.8%	(n=353) 49.0%	<0.001
Possible Peripheral Neuropathy	Abnormal	(n=1,138) 14.4%	(n=390) 21.3%	(n=353) 48.2%	<0.001
Probable Peripheral Neuropathy	Abnormal	(n=1,137) 3.6%	(n=390) 6.4%	(n=353) 21.3%	<0.001
Tremor	Abnormal	(n=1,172) 6.8%	(n=402) 7.7%	(n=368) 7.9%	0.720
Coordination	Abnormal	(n=1,172) 3.2%	(n=402) 6.2%	(n=364) 8.2%	<0.001
Romberg Sign	Abnormal	(n=1,172) 1.0%	(n=402) 2.7%	(n=366) 4.6%	<0.001
Gait	Abnormal	(n=1,172) 6.2%	(n=402) 8.2%	(n=368) 15.5%	<0.001
CNS Index	Abnormal	(n=1,172) 12.7%	(n=402) 15.7%	(n=368) 22.8%	<0.001

| Dependent Variable | Level | Duration of Diabetes (years) | | p-Value |
		Nondiabetic and Newly Diagnosed Diabetic: 0	Previously Diagnosed Diabetic: >0	
Inflammatory Diseases		(n=1,638)	(n=297)	
	Yes	0.9%	0.3%	0.506
Hereditary and Degenerative Diseases	Yes	(n=1,644) 13.9%	(n=299) 21.1%	0.002
Peripheral Disorders		(n=1,640)	(n=297)	
	Yes	22.2%	51.2%	<0.001
Other Neurological Disorders		(n=1,639)	(n=299)	
	Yes	17.0%	24.1%	0.004
Smell		(n=1,642)	(n=299)	
	Abnormal	2.3%	3.3%	0.394
Visual Fields		(n=1,631)	(n=295)	
	Abnormal	0.7%	2.4%	0.022
Light Reaction		(n=1,639)	(n=298)	
	Abnormal	0.7%	0.3%	0.781
Ocular Movement		(n=1,640)	(n=298)	
	Abnormal	0.5%	0.3%	0.999
Facial Sensation		(n=1,643)	(n=299)	
	Abnormal	0.3%	0.7%	0.658
Corneal Reflex		(n=1,637)	(n=297)	
	Abnormal	0.3%	0.7%	0.655
Smile		(n=1,643)	(n=299)	
	Abnormal	0.4%	4.0%	<0.001
Palpebral Fissure		(n=1,642)	(n=299)	
	Abnormal	2.1%	3.7%	0.158
Balance		(n=1,643)	(n=297)	
	Abnormal	1.4%	5.7%	<0.001
Gag Reflex		(n=1,643)	(n=299)	
	Abnormal	0.1%	0.3%	0.951
Speech		(n=1,643)	(n=299)	
	Abnormal	1.0%	1.7%	0.509
Tongue Position Relative to Midline	Deviated	(n=1,643) 0.3%	(n=299) 0.0%	0.738
Shoulder Shrug		(n=1,643)	(n=299)	
	Abnormal	0.3%	1.3%	0.050
Cranial Nerve Index		(n=1,633)	(n=292)	
	Abnormal	8.2%	12.7%	0.018
Pinprick		(n=1,406)	(n=215)	
	Abnormal	6.9%	27.9%	<0.001
Light Touch		(n=1,406)	(n=215)	
	Abnormal	4.0%	18.6%	<0.001

Dependent Variable	Level	Duration of Diabetes (years)		p-Value
		Nondiabetic and Newly Diagnosed Diabetic: 0	Previously Diagnosed Diabetic: >0	
Muscle Status		(n=1,641)	(n=295)	
	Abnormal	4.6%	8.8%	0.004
Patellar Reflex		(n=1,636)	(n=298)	
	Absent	2.6%	8.4%	<0.001
	Sluggish	20.1%	36.2%	
	Active or Very Active	77.3%	55.4%	
Achilles Reflex		(n=1,638)	(n=299)	
	Absent	18.1%	48.2%	<0.001
	Sluggish	36.0%	31.8%	
	Active or Very Active	45.9%	20.1%	
Biceps Reflex		(n=1,642)	(n=299)	
	Absent	1.4%	6.4%	<0.001
	Sluggish	25.0%	40.1%	
	Active or Very Active	73.6%	53.5%	
Babinski Reflex		(n=1,640)	(n=297)	
	Abnormal	1.2%	2.7%	0.090
Any Symmetrical Peripheral Abnormality	Abnormal	(n=1,593) 17.8%	(n=287) 52.6%	<0.001
Possible Peripheral Neuropathy		(n=1,594)	(n=287)	
	Abnormal	16.9%	51.6%	<0.001
Probable Peripheral Neuropathy		(n=1,593)	(n=287)	
	Abnormal	4.5%	24.0%	<0.001
Tremor		(n=1,643)	(n=299)	
	Abnormal	7.0%	8.4%	0.474
Coordination		(n=1,643)	(n=295)	
	Abnormal	3.9%	9.5%	<0.001
Romberg Sign		(n=1,643)	(n=297)	
	Abnormal	1.4%	5.7%	<0.001
Gait		(n=1,643)	(n=299)	
	Abnormal	6.8%	17.4%	<0.001
CNS Index		(n=1,643)	(n=299)	
	Abnormal	13.4%	25.4%	<0.001

Dependent Variable	Level	Composite Exposure to Heavy Metals			Worked with Power Equipment or Tools		
		Yes	No	p-Value	Yes	No	p-Value
Any Symmetrical Peripheral Abnormality	Abnormal	(n=284) 20.8%	(n=1,587) 23.4%	0.365	(n=534) 25.1%	(n=1,342) 22.3%	0.213
Possible Peripheral Neuropathy	Abnormal	(n=285) 20.7%	(n=1,587) 22.4%	0.584	(n=534) 24.3%	(n=1,343) 21.3%	0.170
Probable Peripheral Neuropathy	Abnormal	(n=285) 7.7%	(n=1,586) 7.4%	0.936	(n=534) 8.2%	(n=1,342) 7.2%	0.477

Note: Please see Section 11.1.3 and Table 11-1 for a further discussion of the dependent variables and covariates shown in this appendix.

Table F-4. Dependent Variable-covariate Associations for the Psychology Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Psychoses		(n=886)	(n=1,060)		(n=124)	(n=1,822)	
	Yes	7.2%	5.3%	0.093	11.3%	5.8%	0.024
Alcohol Dependence		(n=885)	(n=1,060)		(n=123)	(n=1,822)	
	Yes	6.2%	5.4%	0.489	6.5%	5.7%	0.868
Drug Dependence		(n=886)	(n=1,060)		(n=124)	(n=1,822)	
	Yes	0.7%	0.1%	0.079	1.6%	0.3%	0.102
Anxiety		(n=883)	(n=1,057)		(n=124)	(n=1,816)	
	Yes	31.6%	26.3%	0.012	29.8%	28.6%	0.854
Other Neuroses		(n=877)	(n=1,051)		(n=123)	(n=1,805)	
	Yes	60.0%	59.0%	0.695	59.4%	59.5%	0.999
SCL-90-R Anxiety		(n=885)	(n=1,058)		(n=124)	(n=1,819)	
	Abnormal	11.3%	6.7%	<0.001	14.5%	8.4%	0.031
SCL-90-R Depression		(n=885)	(n=1,058)		(n=124)	(n=1,819)	
	Abnormal	13.0%	10.7%	0.132	12.9%	11.7%	0.784
SCL-90-R Hostility		(n=885)	(n=1,058)		(n=124)	(n=1,819)	
	Abnormal	7.7%	3.6%	<0.001	8.1%	5.3%	0.264
SCL-90-R Interpersonal Sensitivity		(n=885)	(n=1,058)		(n=124)	(n=1,819)	
	Abnormal	10.9%	8.1%	0.049	15.3%	9.0%	0.028
SCL-90-R Obsessive-compulsive Behavior		(n=885)	(n=1,058)		(n=124)	(n=1,819)	
	Abnormal	16.7%	17.9%	0.548	20.2%	17.2%	0.463
SCL-90-R Paranoid Ideation		(n=885)	(n=1,058)		(n=124)	(n=1,819)	
	Abnormal	5.8%	3.6%	0.030	12.9%	4.0%	<0.001
SCL-90-R Phobic Anxiety		(n=885)	(n=1,058)		(n=124)	(n=1,819)	
	Abnormal	10.2%	6.1%	0.002	16.1%	7.4%	0.001
SCL-90-R Psychoticism		(n=885)	(n=1,058)		(n=124)	(n=1,819)	
	Abnormal	9.8%	9.9%	0.999	17.7%	9.4%	0.004
SCL-90-R Somatization		(n=885)	(n=1,058)		(n=124)	(n=1,819)	
	Abnormal	13.8%	14.6%	0.675	17.7%	14.0%	0.302
SCL-90-R Global Severity Index (GSI)		(n=885)	(n=1,058)		(n=124)	(n=1,819)	
	Abnormal	13.2%	10.1%	0.039	18.6%	11.1%	0.017
SCL-90-R Positive Symptom Total (PST)		(n=885)	(n=1,058)		(n=124)	(n=1,819)	
	Abnormal	13.2%	9.8%	0.023	18.6%	10.9%	0.014
SCL-90-R Positive Symptom Distress Index (PSDI)		(n=885)	(n=1,058)		(n=124)	(n=1,819)	
	Abnormal	8.0%	7.6%	0.770	10.5%	7.6%	0.321
WMS-R: Verbal Paired Associates		(n=1,942)			(n=124)	(n=1,818)	
	--	r = -0.148		<0.001	O = 10.45	O = 11.02	0.054
WMS-R: Logical Memory, Immediate Recall		(n=1,942)			(n=124)	(n=1,818)	
	--	r = -0.109		<0.001	O = 10.94	O = 11.68	0.017
WMS-R: Logical Memory, Delayed Recall		(n=1,941)			(n=124)	(n=1,817)	
	--	r = -0.106		<0.001	O = 8.21	O = 9.56	<0.001

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
WMS-R: Visual Reproduction, Immediate Recall	--	(n=1,940)			(n=123)	(n=1,817)	
		r = -0.278		<0.001	O = 26.41	O = 27.98	<0.001
WMS-R: Visual Reproduction, Delayed Recall	--	(n=1,940)			(n=123)	(n=1,817)	
		r = -0.290		<0.001	O = 24.02	O = 26.34	<0.001

Dependent Variable	Level	Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Alcohol Dependence	Present	(n=768) 3.0%	(n=318) 7.9%	(n=860) 8.4%	<0.001
Drug Dependence	Present	(n=768) 4.0%	(n=318) 6.6%	(n=859) 7.0%	0.030
Anxiety	Present	(n=768) 0.1%	(n=318) 0.0%	(n=860) 0.7%	0.081
Other Neuroses	Present	(n=768) 18.2%	(n=317) 32.5%	(n=855) 36.7%	<0.001
SCL-90-R Anxiety	Present	(n=764) 48.3%	(n=315) 67.9%	(n=849) 66.3%	<0.001
SCL-90-R Depression	Abnormal	(n=768) 3.8%	(n=318) 10.1%	(n=857) 12.8%	<0.001
SCL-90-R Hostility	Abnormal	(n=768) 7.4%	(n=318) 11.0%	(n=857) 15.9%	<0.001
SCL-90-R Interpersonal Sensitivity	Abnormal	(n=768) 2.1%	(n=318) 7.6%	(n=857) 7.7%	<0.001
SCL-90-R Obsessive-compulsive Behavior	Abnormal	(n=768) 5.3%	(n=318) 11.6%	(n=857) 12.1%	<0.001
SCL-90-R Paranoid Ideation	Abnormal	(n=768) 11.2%	(n=318) 19.5%	(n=857) 22.1%	<0.001
SCL-90-R Phobic Anxiety	Abnormal	(n=768) 1.8%	(n=318) 4.1%	(n=857) 7.2%	<0.001
SCL-90-R Psychoticism	Abnormal	(n=768) 2.9%	(n=318) 10.7%	(n=857) 11.6%	<0.001
SCL-90-R Somatization	Abnormal	(n=768) 6.3%	(n=318) 10.4%	(n=857) 13.0%	<0.001
SCL-90-R Global Severity Index (GSI)	Abnormal	(n=768) 7.3%	(n=318) 18.9%	(n=857) 18.7%	<0.001
SCL-90-R Positive Symptom Total (PST)	Abnormal	(n=768) 5.7%	(n=318) 11.3%	(n=857) 16.8%	<0.001
SCL-90-R Positive Symptom Distress Index (PSDI)	Abnormal	(n=768) 6.9%	(n=318) 10.4%	(n=857) 15.8%	<0.001
	Abnormal	(n=768) 3.0%	(n=318) 12.0%	(n=857) 10.5%	<0.001

Dependent Variable	Level	Occupation			p-Value
		Officer	Enlisted Flyer	Enlisted Groundcrew	
WMS-R: Verbal Paired Associates		(n=768)	(n=317)	(n=857)	
	--	O = 11.58	O = 10.13	O = 10.76	<0.001
WMS-R: Logical Memory, Immediate Recall		(n=768)	(n=317)	(n=857)	
	--	O = 12.60	O = 10.81	O = 11.06	<0.001
WMS-R: Logical Memory, Delayed Recall		(n=767)	(n=317)	(n=857)	
	--	O = 10.62	O = 8.50	O = 8.81	<0.001
WMS-R: Visual Reproduction, Immediate Recall		(n=768)	(n=316)	(n=856)	
	--	O = 28.79	O = 26.26	O = 27.66	<0.001
WMS-R: Visual Reproduction, Delayed Recall		(n=768)	(n=316)	(n=856)	
	--	O = 27.41	O =24.29	O = 25.79	<0.001

Dependent Variable	Level	Education			Current Alcohol Use (drinks/day)		
		College	High School	p-Value	0–1	>1	p-Value
Psychoses		(n=1,048)	(n=896)		--	--	--
	Yes	4.5%	8.2%	0.001			
Alcohol Dependence		(n=1,048)	(n=895)		--	--	--
	Yes	5.2%	6.5%	0.249			
Drug Dependence		(n=1,048)	(n=896)		--	--	--
	Yes	0.3%	0.5%	0.835			
Anxiety		(n=1,046)	(n=892)		--	--	--
	Yes	24.3%	34.0%	<0.001			
Other Neuroses		(n=1,043)	(n=883)		--	--	--
	Yes	52.5%	67.5%	<0.001			
SCL-90-R Anxiety		(n=1,048)	(n=894)		(n=1,651)	(n=291)	
	Abnormal	5.9%	12.2%	<0.001	9.1%	7.2%	0.355
SCL-90-R Depression		(n=1,048)	(n=894)		(n=1,651)	(n=291)	
	Abnormal	8.1%	16.0%	<0.001	11.8%	11.7%	0.999
SCL-90-R Hostility		(n=1,048)	(n=894)		(n=1,651)	(n=291)	
	Abnormal	3.6%	7.6%	<0.001	5.4%	5.8%	0.863
SCL-90-R Interpersonal Sensitivity		(n=1,048)	(n=894)		(n=1,651)	(n=291)	
	Abnormal	6.9%	12.3%	<0.001	9.3%	10.0%	0.789
SCL-90-R Obsessive-compulsive Behavior		(n=1,048)	(n=894)		(n=1,651)	(n=291)	
	Abnormal	13.0%	22.5%	<0.001	17.8%	15.1%	0.314
SCL-90-R Paranoid Ideation		(n=1,048)	(n=894)		(n=1,651)	(n=291)	
	Abnormal	2.7%	6.8%	<0.001	4.4%	5.5%	0.511
SCL-90-R Phobic Anxiety		(n=1,048)	(n=894)		(n=1,651)	(n=291)	
	Abnormal	4.8%	11.7%	<0.001	8.4%	5.8%	0.179
SCL-90-R Psychoticism		(n=1,048)	(n=894)		(n=1,651)	(n=291)	
	Abnormal	7.2%	13.1%	<0.001	9.4%	12.7%	0.100

Dependent Variable	Level	Education			Current Alcohol Use (drinks/day)		
		College	High School	p-Value	0–1	>1	p-Value
SCL-90-R Somatization	Abnormal	(n=1,048) 10.0%	(n=894) 19.0%	<0.001	(n=1,651) 14.8%	(n=291) 10.7%	0.077
SCL-90-R Global Severity Index (GSI)	Abnormal	(n=1,048) 7.8%	(n=894) 15.9%	<0.001	(n=1,651) 11.8%	(n=291) 10.0%	0.418
SCL-90-R Positive Symptom Total (PST)	Abnormal	(n=1,048) 8.4%	(n=894) 14.9%	<0.001	(n=1,651) 11.5%	(n=291) 11.0%	0.902
SCL-90-R Positive Symptom Distress Index (PSDI)	Abnormal	(n=1,048) 4.5%	(n=894) 11.6%	<0.001	(n=1,651) 8.1%	(n=291) 5.8%	0.224
WMS-R: Verbal Paired Associates	--	(n=1,048) $\bar{O}$ = 11.43	(n=893) $\bar{O}$ = 10.47	<0.001	(n=1,941) r = -0.001		0.976
WMS-R: Logical Memory, Immediate Recall	--	(n=1,048) $\bar{O}$ = 12.32	(n=893) $\bar{O}$ = 10.82	<0.001	(n=1,941) r =0.059		0.009
WMS-R: Logical Memory, Delayed Recall	--	(n=1,047) $\bar{O}$ = 10.30	(n=893) $\bar{O}$ = 8.51	<0.001	(n=1,940) r = 0.064		0.005
WMS-R: Visual Reproduction, Immediate Recall	--	(n=1,047) $\bar{O}$ = 28.58	(n=892) $\bar{O}$ = 27.06	<0.001	(n=1,939) r = 0.064		0.005
WMS-R: Visual Reproduction, Delayed Recall	--	(n=1,047) $\bar{O}$ = 27.18	(n=892) $\bar{O}$ = 25.03	<0.001	(n=1,939) r = 0.067		0.003

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	>0-40	>40	p-Value
Psychoses	Present	(n=107) 5.6%	(n=1,231) 5.1%	(n=599) 8.4%	0.025
Drug Dependence	Present	(n=107) 0.0%	(n=1,231) 0.2%	(n=599) 0.7%	0.298
Anxiety	Present	(n=107) 30.8%	(n=1,227) 27.9%	(n=597) 29.8%	0.603
Other Neuroses	Present	(n=107) 58.9%	(n=1,221) 55.6%	(n=591) 67.2%	<0.001
SCL-90-R Anxiety	Abnormal	(n=107) 11.2%	(n=1,230) 8.1%	(n=598) 9.5%	0.362
SCL-90-R Depression	Abnormal	(n=107) 14.0%	(n=1,230) 10.1%	(n=598) 14.4%	0.020
SCL-90-R Hostility	Abnormal	(n=107) 2.8%	(n=1,230) 4.8%	(n=598) 7.2%	0.050
SCL-90-R Interpersonal Sensitivity	Abnormal	(n=107) 9.4%	(n=1,230) 8.3%	(n=598) 11.2%	0.131
SCL-90-R Obsessive-compulsive Behavior	Abnormal	(n=107) 19.6%	(n=1,230) 15.0%	(n=598) 21.4%	0.002

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	**>0-40**	**>40**	**p-Value**
SCL-90-R Paranoid Ideation		(n=107)	(n=1,230)	(n=598)	
	Abnormal	5.6%	3.5%	6.5%	0.012
SCL-90-R Phobic Anxiety		(n=107)	(n=1,230)	(n=598)	
	Abnormal	11.2%	7.2%	8.9%	0.191
SCL-90-R Psychoticism		(n=107)	(n=1,230)	(n=598)	
	Abnormal	9.4%	8.5%	12.9%	0.012
SCL-90-R Somatization		(n=107)	(n=1,230)	(n=598)	
	Abnormal	20.6%	12.9%	15.2%	0.058
SCL-90-R Global Severity Index (GSI)		(n=107)	(n=1,230)	(n=598)	
	Abnormal	15.9%	9.6%	14.4%	0.003
SCL-90-R Positive Symptom Total (PST)		(n=107)	(n=1,230)	(n=598)	
	Abnormal	12.2%	9.8%	14.1%	0.027
SCL-90-R Positive Symptom Distress Index (PSDI)		(n=107)	(n=1,230)	(n=598)	
	Abnormal	11.2%	7.2%	8.2%	0.299
WMS-R: Verbal Paired Associates			(n=1,934)		
	--		r = -0.033		0.141
WMS-R: Logical Memory, Immediate Recall			(n=1,934)		
	--		r = -0.038		0.095
WMS-R: Logical Memory, Delayed Recall			(n=1,933)		
	--		r = -0.042		0.068
WMS-R: Visual Reproduction, Immediate Recall			(n=1,932)		
	--		r =-0.072		0.002
WMS-R: Visual Reproduction, Delayed Recall			(n=1,932)		
	--		r = -0.076		<0.001

Dependent Variable	Level	Current Total Household Income			Current Employment		
		<$65,000	**≥$65,000**	**p-Value**	**Yes**	**No**	**p-Value**
Psychoses		(n=861)	(n=1,030)		(n=1,081)	(n=862)	
	Yes	8.8%	3.8%	<0.001	4.4%	8.5%	<0.001
Alcohol Dependence		(n=860)	(n=1,030)		(n=1,081)	(n=861)	
	Yes	8.0%	3.7%	<0.001	5.1%	6.6%	0.180
Drug Dependence		(n=861)	(n=1,030)		(n=1,081)	(n=862)	
	Yes	0.7%	0.1%	0.079	0.5%	0.2%	0.644
Anxiety		(n=857)	(n=1,028)		(n=1,080)	(n=857)	
	Yes	35.0%	23.6%	<0.001	28.7%	28.8%	0.995
Other Neuroses		(n=853)	(n=1,020)		(n=1,074)	(n=851)	
	Yes	68.6%	51.5%	<0.001	56.5%	63.1%	0.004
SCL-90-R Anxiety		(n=860)	(n=1,030)		(n=1,080)	(n=861)	
	Abnormal	13.3%	5.2%	<0.001	7.6%	10.3%	0.042
SCL-90-R Depression		(n=860)	(n=1,030)		(n=1,080)	(n=861)	
	Abnormal	17.4%	7.3%	<0.001	9.4%	14.8%	<0.001

Dependent Variable	Level	Current Total Household Income			Current Employment		
		<$65,000	≥$65,000	p-Value	Yes	No	p-Value
SCL-90-R Hostility		(n=860)	(n=1,030)		(n=1,080)	(n=861)	
	Abnormal	8.0%	3.6%	<0.001	4.2%	7.1%	0.007
SCL-90-R Interpersonal Sensitivity		(n=860)	(n=1,030)		(n=1,080)	(n=861)	
	Abnormal	13.5%	6.0%	<0.001	7.3%	12.0%	<0.001
SCL-90-R Obsessive-compulsive Behavior		(n=860)	(n=1,030)		(n=1,080)	(n=861)	
	Abnormal	23.3%	12.3%	<0.001	13.6%	22.1%	<0.001
SCL-90-R Paranoid Ideation		(n=860)	(n=1,030)		(n=1,080)	(n=861)	
	Abnormal	7.3%	2.2%	<0.001	3.4%	6.0%	0.009
SCL-90-R Phobic Anxiety		(n=860)	(n=1,030)		(n=1,080)	(n=861)	
	Abnormal	11.4%	5.2%	<0.001	6.9%	9.4%	0.048
SCL-90-R Psychoticism		(n=860)	(n=1,030)		(n=1,080)	(n=861)	
	Abnormal	13.5%	6.9%	<0.001	7.3%	13.1%	<0.001
SCL-90-R Somatization		(n=860)	(n=1,030)		(n=1,080)	(n=861)	
	Abnormal	19.8%	9.3%	<0.001	11.3%	17.8%	<0.001
SCL-90-R Global Severity Index (GSI)		(n=860)	(n=1,030)		(n=1,080)	(n=861)	
	Abnormal	16.5%	7.4%	<0.001	9.4%	14.2%	0.002
SCL-90-R Positive Symptom Total (PST)		(n=860)	(n=1,030)		(n=1,080)	(n=861)	
	Abnormal	16.1%	7.7%	<0.001	9.9%	13.2%	0.026
SCL-90-R Positive Symptom Distress Index (PSDI)		(n=860)	(n=1,030)		(n=1,080)	(n=861)	
	Abnormal	12.4%	4.1%	<0.001	5.1%	11.2%	<0.001
WMS-R: Verbal Paired Associates		(n=1,888)			(n=1,080)	(n=860)	
	--	r = 0.134		<0.001	Ō = 11.38	Ō = 10.50	<0.001
WMS-R: Logical Memory, Immediate Recall		(n=1,888)			(n=1,080)	(n=860)	
	--	r = 0.199		<0.001	Ō = 12.06	Ō = 11.09	<0.001
WMS-R: Logical Memory, Delayed Recall		(n=1,887)			(n=1,079)	(n=860)	
	--	r = 0.216		<0.001	Ō = 9.98	Ō = 8.85	<0.001
WMS-R: Visual Reproduction, Immediate Recall		(n=1,887)			(n=1,080)	(n=858)	
	--	r = 0.223		<0.001	Ō = 28.60	Ō = 26.97	<0.001
WMS-R: Visual Reproduction, Delayed Recall		(n=1,887)			(n=1,080)	(n=858)	
	--	r = 0.247		<0.001	Ō = 27.34	Ō = 24.74	<0.001

Dependent Variable	Level	Current Marital Status			Current Parental Status		
		Married	Not Married	p-Value	Child < 18 Years Old Living at Home	No Child < 18 Years Old Living at Home	p-Value
Psychoses		(n=1,645)	(n=298)		(n=187)	(n=1,757)	
	Yes	5.2%	11.4%	<0.001	7.5%	6.0%	0.532
Alcohol Dependence		(n=1,645)	(n=297)		(n=187)	(n=1,756)	
	Yes	4.7%	11.8%	<0.001	7.0%	5.6%	0.570

Dependent Variable	Level	Current Marital Status			Current Parental Status		
		Married	Not Married	p-Value	Child < 18 Years Old Living at Home	No Child < 18 Years Old Living at Home	p-Value
Drug Dependence		(n=1,645)	(n=298)		(n=187)	(n=1,757)	
	Yes	0.1%	2.0%	<0.001	0.5%	0.3%	0.999
Anxiety		(n=1,641)	(n=296)		(n=186)	(n=1,752)	
	Yes	27.5%	35.5%	0.007	31.7%	28.4%	0.390
Other Neuroses		(n=1,631)	(n=294)		(n=186)	(n=1,740)	
	Yes	57.1%	72.1%	<0.001	67.2%	58.6%	0.028
SCL-90-R Anxiety		(n=1,643)	(n=298)		(n=187)	(n=1,755)	
	Abnormal	8.0%	13.1%	0.007	12.3%	8.4%	0.101
SCL-90-R Depression		(n=1,643)	(n=298)		(n=187)	(n=1,755)	
	Abnormal	10.8%	17.1%	0.002	13.9%	11.5%	0.397
SCL-90-R Hostility		(n=1,643)	(n=298)		(n=187)	(n=1,755)	
	Abnormal	5.2%	6.7%	0.371	8.0%	5.2%	0.146
SCL-90-R Interpersonal Sensitivity		(n=1,643)	(n=298)		(n=187)	(n=1,755)	
	Abnormal	8.6%	13.8%	0.007	9.1%	9.4%	0.995
SCL-90-R Obsessive-compulsive Behavior		(n=1,643)	(n=298)		(n=187)	(n=1,755)	
	Abnormal	16.1%	24.2%	0.001	19.8%	17.1%	0.411
SCL-90-R Paranoid Ideation		(n=1,643)	(n=298)		(n=187)	(n=1,755)	
	Abnormal	3.9%	8.4%	0.001	5.9%	4.4%	0.478
SCL-90-R Phobic Anxiety		(n=1,643)	(n=298)		(n=187)	(n=1,755)	
	Abnormal	7.4%	11.1%	0.043	11.8%	7.6%	0.062
SCL-90-R Psychoticism		(n=1,643)	(n=298)		(n=187)	(n=1,755)	
	Abnormal	8.7%	16.4%	<0.001	11.8%	9.7%	0.438
SCL-90-R Somatization		(n=1,643)	(n=298)		(n=187)	(n=1,755)	
	Abnormal	13.8%	16.4%	0.257	15.0%	14.1%	0.822
SCL-90-R Global Severity Index (GSI)		(n=1,643)	(n=298)		(n=187)	(n=1,755)	
	Abnormal	10.8%	15.8%	0.017	13.4%	11.3%	0.480
SCL-90-R Positive Symptom Total (PST)		(n=1,643)	(n=298)		(n=187)	(n=1,755)	
	Abnormal	10.5%	16.1%	0.007	11.2%	11.4%	0.999
SCL-90-R Positive Symptom Distress Index (PSDI)		(n=1,643)	(n=298)		(n=187)	(n=1,755)	
	Abnormal	7.4%	10.1%	0.138	8.0%	7.8%	0.999
WMS-R: Verbal Paired Associates		(n=1,642)	(n=298)		(n=187)	(n=1,755)	
	--	O = 11.00	O = 10.92	0.710	O = 11.20	O = 10.97	0.340
WMS-R: Logical Memory, Immediate Recall		(n=1,642)	(n=298)		(n=187)	(n=1,754)	
	--	O = 11.69	O = 11.30	0.062	O = 11.88	O = 11.60	0.275
WMS-R: Logical Memory, Delayed Recall		(n=1,641)	(n=298)		(n=187)	(n=1,753)	
	--	O = 9.57	O = 8.96	0.009	O = 9.78	O = 9.44	0.231

Dependent Variable	Level	Current Marital Status			Current Parental Status		
		Married	Not Married	p-Value	Child < 18 Years Old Living at Home	No Child < 18 Years Old Living at Home	p-Value
WMS-R: Visual Repro- duction, Immediate Recall	--	(n=1,640) O = 28.01	(n=298) O = 27.14	0.004	(n=187) O = 28.65	(n=1,752) O = 27.80	0.022
WMS-R: Visual Repro- duction, Delayed Recall	--	(n=1,640) O = 26.39	(n=298) O = 25.11	0.001	(n=187) O = 27.10	(n=1,752) O = 26.10	0.042

--: The covariate was not applicable for this dependent variable.

Note: Correlations (r) are based on total sample size and are not category-specific.

Please see Section 12.1.3 and Table 12-1 for a further discussion of the dependent variables and covariates shown in this appendix.

Table F-5. Dependent Variable-covariate Associations for the Gastrointestinal Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Uncharacterized Hepatitis		(n=886)	(n=1,053)		(n=125)	(n=1,814)	
	Yes	1.7%	1.4%	0.770	1.6%	1.5%	0.999
Jaundice (unspecified)		(n=874)	(n=1,028)		(n=124)	(n=1,778)	
	Yes	2.3%	2.6%	0.745	1.6%	2.5%	0.736
Chronic Liver Disease and Cirrhosis (alcohol-related)		(n=843)	(n=997)		(n=113)	(n=1,727)	
	Yes	4.3%	4.2%	0.999	5.3%	4.2%	0.732
Chronic Liver Disease and Cirrhosis (nonalcohol-related)		(n=890)	(n=1,061)		(n=125)	(n=1,826)	
	Yes	2.9%	2.6%	0.810	2.4%	2.8%	0.999
Liver Abscess and Sequelae of Chronic Liver Disease		(n=890)	(n=1,061)		(n=125)	(n=1,826)	
	Yes	0.2%	0.5%	0.598	0.0%	0.4%	0.999
Enlarged Liver (hepatomegaly)		(n=889)	(n=1,060)		(n=124)	(n=1,825)	
	Yes	3.0%	4.3%	0.198	3.2%	3.7%	0.968
Other Disorders of the Liver		(n=885)	(n=1,054)		(n=125)	(n=1,814)	
	Yes	47.8%	44.5%	0.160	72.8%	44.2%	<0.001
Current Hepatomegaly		(n=873)	(n=1,052)		(n=117)	(n=1,808)	
	Yes	1.2%	1.4%	0.735	0.9%	1.3%	0.987
AST		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = -0.031		0.178	O = 24.61	O = 24.28	0.649
(discrete)	High	8.8%	6.8%	0.140	8.6%	7.7%	0.861
ALT		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = -0.245		<0.001	O = 44.19	O = 44.69	0.662
(discrete)	High	11.1%	4.4%	<0.001	8.6%	7.3%	0.755
GGT		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = -0.168		<0.001	O = 50.82	O = 45.04	0.016
(discrete)	High	13.2%	8.5%	<0.001	9.4%	10.7%	0.776
Alkaline Phosphatase		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = -0.083		<0.001	O = 94.88	O = 93.11	0.452
(discrete)	High	8.3%	5.8%	0.040	9.4%	6.8%	0.366
Total Bilirubin		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = 0.073		0.001	O = 0.445	O = 0.523	<0.001
(discrete)	High	6.6%	6.6%	0.999	6.8%	6.5%	0.999
Direct Bilirubin		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
	High	0.4%	1.0%	0.184	1.7%	0.6%	0.410
LDH		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = 0.105		<0.001	O = 157.7	O = 152.5	0.053
(discrete)	High	7.9%	11.8%	0.007	14.5%	9.8%	0.132
Cholesterol		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[b]	--	r = -0.175		<0.001	O = 198.7	O = 196.3	0.500
(discrete)	High	16.6%	8.8%	<0.001	15.4%	12.1%	0.373

Table F-5. Dependent Variable-covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
HDL Cholesterol		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = 0.068		0.003	O = 47.03	O = 44.34	0.019
(discrete)	Low	17.0%	15.6%	0.424	7.7%	16.8%	0.014
Cholesterol-HDL Ratio		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = -0.177		<0.001	O = 4.18	O = 4.39	0.067
(discrete)	High	38.3%	26.9%	<0.001	19.7%	32.9%	0.004
Triglycerides		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = -0.127		<0.001	O = 104.5	O = 136.2	<0.001
(discrete)	High	14.5%	8.6%	<0.001	6.0%	11.6%	0.088
Creatine Phosphokinase		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = -0.080		<0.001	O = 201.8	O = 102.5	<0.001
(discrete)	High	10.0%	10.0%	0.999	40.2%	8.0%	<0.001
Serum Amylase		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = 0.051		0.025	O = 68.30	O = 54.27	<0.001
(discrete)	High	2.4%	3.7%	0.138	6.8%	2.9%	0.035
Antibodies for Hepatitis A		(n=888)	(n=1,059)		(n=125)	(n=1,822)	
	Yes	24.9%	41.3%	<0.001	46.4%	32.9%	0.003
Serological Evidence of Prior Hepatitis B Infection		(n=890)	(n=1,061)		(n=125)	(n=1,826)	
	Yes	8.8%	9.5%	0.619	21.6%	8.3%	<0.001
Antibodies for Hepatitis C		(n=890)	(n=1,061)		(n=125)	(n=1,826)	
	Yes	1.8%	0.8%	0.061	5.6%	0.9%	<0.001
Stool Hemoccult		(n=810)	(n=990)		(n=104)	(n=1,696)	
	Yes	1.9%	1.2%	0.360	1.0%	1.5%	0.960
Protein Profile: Prealbumin		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[b]	--	r = -0.134		<0.001	O = 28.59	O = 28.89	0.585
(discrete)	Low	1.4%	1.8%	0.581	0.9%	1.7%	0.769
Protein Profile: Albumin		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)	--	r = -0.096		<0.001	O = 4,080.3	O = 4,194.3	<0.001
(discrete)	Low	0.5%	0.7%	0.774	2.6%	0.4%	0.021
Protein Profile: α-1-Acid Glycoprotein		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = -0.023		0.322	O = 77.48	O = 78.31	0.645
(discrete)	High	5.2%	5.3%	0.973	6.0%	5.2%	0.881
Protein Profile: α-1-Antitrypsin		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[b]	--	r = 0.100		<0.001	O = 138.3	O = 141.1	0.253
(discrete)	Low	1.5%	1.4%	0.547	0.0%	1.6%	0.052
	Normal	88.8%	87.4%		94.9%	87.6%	
	High	9.7%	11.2%		5.1%	10.9%	

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Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Protein Profile: α-2- Macroglobulin		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = 0.331		<0.001	Ō = 161.7	Ō = 187.6	<0.001
(discrete)	High	6.9%	19.8%	<0.001	6.0%	14.5%	0.015
Protein Profile: Apolipoprotein B		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[b]	--	r = -0.169		<0.001	Ō = 103.1	Ō = 102.7	0.842
(discrete)	High	2.1%	1.6%	0.566	1.7%	1.8%	0.999
Protein Profile: C3 Complement		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[b]	--	r = -0.092		<0.001	Ō = 126.0	Ō = 119.1	<0.001
(discrete)	Low	0.9%	2.2%	0.045	0.0%	1.7%	0.294
Protein Profile: C4 Complement		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[b]	--	r = -0.047		0.039	Ō = 26.97	Ō = 22.34	<0.001
(discrete)	Low	6.8%	8.5%	0.202	4.3%	7.9%	0.209
Protein Profile: Haptoglobin		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[b]	--	r = 0.053		0.021	Ō = 119.3	Ō = 122.3	0.602
(discrete)	High	11.5%	13.4%	0.241	12.0%	12.6%	0.961
Protein Profile: Transferrin		(n=869)	(n=1,053)		(n=117)	(n=1,805)	
(continuous)[a]	--	r = -0.082		<0.001	Ō = 243.1	Ō = 255.3	0.001
(discrete)	Low	3.9%	7.6%	<0.001	8.6%	5.8%	0.301
Prothrombin Time		(n=740)	(n=726)		(n=102)	(n=1,364)	
(continuous)[a]	--	r = 0.117		<0.001	Ō = 10.73	Ō = 10.72	0.900
(discrete)	High	0.3%	1.5%	0.024	2.0%	0.8%	0.514

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Uncharacterized Hepatitis		(n=762)	(n=318)	(n=859)	
	Yes	1.2%	1.3%	2.0%	0.387
Jaundice (unspecified)		(n=746)	(n=310)	(n=846)	
	Yes	3.1%	1.0%	2.5%	0.131
Chronic Liver Disease and Cirrhosis (alcohol-related)		(n=737)	(n=298)	(n=805)	
	Yes	3.1%	3.7%	5.5%	0.065
Chronic Liver Disease and Cirrhosis (nonalcohol-related)		(n=769)	(n=318)	(n=864)	
	Yes	2.5%	2.5%	3.1%	0.692
Liver Abscess and Sequelae of Chronic Liver Disease		(n=769)	(n=318)	(n=864)	
	Yes	0.4%	0.0%	0.5%	0.490
Enlarged Liver (hepatomegaly)		(n=768)	(n=318)	(n=863)	
	Yes	3.3%	3.5%	4.2%	0.601
Other Disorders of the Liver		(n=761)	(n=318)	(n=860)	
	Yes	43.8%	49.1%	46.9%	0.224

Table F-5. Dependent Variable-covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Current Hepatomegaly		(n=765)	(n=314)	(n=846)	
	Yes	1.3%	1.3%	1.3%	0.999
AST		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	Ô = 24.74	Ô = 23.55	Ô = 24.18	0.055
(discrete)	High	7.7%	6.7%	8.1%	0.739
ALT		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	Ô = 44.11	Ô = 43.38	Ô = 45.65	0.004
(discrete)	High	6.0%	8.6%	8.2%	0.172
GGT		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	Ô = 43.38	Ô = 44.96	Ô = 47.42	0.003
(discrete)	High	9.6%	11.5%	11.3%	0.470
Alkaline Phosphatase		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	Ô = 89.08	Ô = 95.50	Ô = 96.25	<0.001
(discrete)	High	4.5%	9.9%	8.1%	0.001
Total Bilirubin		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	Ô = 0.555	Ô = 0.493	Ô = 0.495	<0.001
(discrete)	High	7.1%	5.4%	6.5%	0.607
Direct Bilirubin		(n=764)	(n=314)	(n=844)	
	High	0.9%	0.0%	0.7%	0.246
LDH		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	Ô = 153.3	Ô = 151.8	Ô = 152.6	0.713
(discrete)	High	10.6%	10.5%	9.4%	0.679
Cholesterol		(n=764)	(n=314)	(n=844)	
(continuous)[b]	--	Ô = 193.1	Ô = 197.7	Ô = 199.1	0.003
(discrete)	High	8.9%	13.4%	15.1%	<0.001
HDL Cholesterol		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	Ô = 47.09	Ô = 43.34	Ô = 42.70	<0.001
(discrete)	Low	12.7%	17.5%	19.0%	0.003
Cholesterol-HDL Ratio		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	Ô = 4.07	Ô = 4.52	Ô = 4.62	<0.001
(discrete)	High	23.4%	34.7%	38.9%	<0.001
Triglycerides		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	Ô = 122.4	Ô = 141.6	Ô = 142.5	<0.001
(discrete)	High	7.7%	11.8%	14.2%	<0.001
Creatine Phosphokinase		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	Ô = 103.0	Ô = 101.1	Ô = 112.6	0.003
(discrete)	High	8.1%	11.2%	11.3%	0.084

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Serum Amylase		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	O = 54.69	O = 55.04	O = 55.34	0.833
(discrete)	High	2.5%	3.5%	3.6%	0.429
Antibodies for Hepatitis A		(n=766)	(n=318)	(n=863)	
	Yes	27.9%	46.2%	34.4%	<0.001
Serological Evidence of Prior Hepatitis B Infection		(n=769)	(n=318)	(n=864)	
	Yes	4.2%	14.8%	11.6%	<0.001
Antibodies for Hepatitis C		(n=769)	(n=318)	(n=864)	
	Yes	0.4%	1.3%	2.0%	0.016
Stool Hemoccult		(n=715)	(n=296)	(n=789)	
	Yes	1.0%	1.7%	1.9%	0.326
Protein Profile: Prealbumin		(n=764)	(n=314)	(n=844)	
(continuous)[b]	--	O = 28.97	O = 28.57	O = 28.90	0.567
(discrete)	Low	1.7%	1.3%	1.7%	0.871
Protein Profile: Albumin		(n=764)	(n=314)	(n=844)	
(continuous)	--	O = 4,169.2	O = 4,201.9	O = 4,198.3	0.063
(discrete)	Low	0.7%	0.6%	0.5%	0.879
Protein Profile: α-1-Acid Glycoprotein		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	O = 75.51	O = 79.84	O = 80.24	<0.001
(discrete)	High	4.1%	5.7%	6.2%	0.154
Protein Profile: α-1-Antitrypsin		(n=764)	(n=314)	(n=844)	
(continuous)[b]	--	O = 136.9	O = 146.8	O = 142.5	<0.001
(discrete)	Low	2.1%	0.3%	1.3%	0.001
	Normal	90.5%	85.4%	86.9%	
	High	7.5%	14.3%	11.9%	
Protein Profile: α-2-Macroglobulin		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	O = 185.4	O = 197.6	O = 182.3	<0.001
(discrete)	High	13.2%	16.9%	13.5%	0.256
Protein Profile: Apolipoprotein B		(n=764)	(n=314)	(n=844)	
(continuous)[b]	--	O = 99.1	O = 104.7	O = 105.3	<0.001
(discrete)	High	1.8%	1.9%	1.8%	0.988
Protein Profile: C3 Complement		(n=764)	(n=314)	(n=844)	
(continuous)[b]	--	O = 113.4	O = 122.4	O = 124.0	<0.001
(discrete)	Low	2.6%	1.9%	0.6%	0.005
Protein Profile: C4 Complement		(n=764)	(n=314)	(n=844)	
(continuous)[b]	--	O = 21.94	O = 22.64	O = 23.22	<0.001
(discrete)	Low	8.4%	9.6%	6.4%	0.134

Table F-5. Dependent Variable-covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Military Occupation			p-Value
		Officer	Enlisted Flyer	Enlisted Groundcrew	
Protein Profile: Haptoglobin		(n=764)	(n=314)	(n=844)	
(continuous)[b]	--	O = 111.2	O = 133.7	O = 128.2	<0.001
(discrete)	High	9.0%	16.9%	14.1%	<0.001
Protein Profile: Transferrin		(n=764)	(n=314)	(n=844)	
(continuous)[a]	--	O = 250.4	O = 256.0	O = 257.7	0.001
(discrete)	Low	7.1%	7.0%	4.5%	0.064
Prothrombin Time		(n=574)	(n=226)	(n=666)	
(continuous)[a]	--	O = 10.76	O = 10.73	O = 10.69	0.055
(discrete)	High	0.9%	2.2%	0.5%	0.051

Dependent Variable	Level	Cumulative Degreasing Chemical Exposure			Cumulative Industrial Chemical Exposure		
		Yes	No	p-Value	Yes	No	p-Value
Uncharacterized Hepatitis		(n=1,252)	(n=687)		(n=1,212)	(n=727)	
	Yes	1.8%	1.0%	0.229	2.0%	0.8%	0.071
Jaundice (unspecified)		(n=1,229)	(n=673)		(n=1,189)	(n=713)	
	Yes	2.5%	2.4%	0.968	2.4%	2.7%	0.788
Chronic Liver Disease and Cirrhosis (alcohol-related)	Yes	(n=1,187) 4.8%	(n=653) 3.2%	0.135	(n=1,147) 5.1%	(n=693) 2.9%	0.034
Chronic Liver Disease and Cirrhosis (nonalcohol-related)	Yes	(n=1,259) 3.1%	(n=692) 2.2%	0.292	(n=1,217) 3.0%	(n=734) 2.3%	0.423
Liver Abscess and Sequelae of Chronic Liver Disease	Yes	(n=1,259) 0.3%	(n=692) 0.4%	0.989	(n=1,217) 0.3%	(n=734) 0.5%	0.498
Enlarged Liver (hepatomegaly)		(n=1,257)	(n=692)		(n=1,216)	(n=733)	
	Yes	4.1%	3.0%	0.308	4.0%	3.3%	0.523
Other Disorders of the Liver		(n=1,250)	(n=689)		(n=1,212)	(n=727)	
	Yes	46.8%	44.6%	0.368	45.6%	46.6%	0.703
AST		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	O = 24.31	O = 24.27	0.918	O = 24.01	O = 24.78	0.034
(discrete)	High	7.8%	7.6%	0.976	6.9%	9.1%	0.099
ALT		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	O = 45.05	O = 43.96	0.056	O = 44.62	O = 44.73	0.847
(discrete)	High	8.0%	6.3%	0.200	7.0%	8.0%	0.513
GGT		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	O = 45.61	O = 44.95	0.556	O = 45.09	O = 45.85	0.493
(discrete)	High	10.3%	11.3%	0.546	10.6%	10.7%	0.985
Alkaline Phosphatase		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	O = 94.11	O = 91.62	0.032	O = 93.70	O = 92.43	0.273
(discrete)	High	7.4%	6.1%	0.364	7.0%	6.9%	0.999

Table F-5. Dependent Variable-covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Cumulative Degreasing Chemical Exposure			Cumulative Industrial Chemical Exposure		
		Yes	No	p-Value	Yes	No	p-Value
Total Bilirubin		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	O = 0.504	O = 0.544	<0.001	O = 0.509	O = 0.533	0.043
(discrete)	High	6.5%	6.6%	0.999	7.0%	5.9%	0.415
Direct Bilirubin		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
	High	0.7%	0.6%	0.941	0.6%	0.8%	0.744
LDH		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	O = 153.2	O = 151.9	0.321	O = 152.6	O = 153.1	0.706
(discrete)	High	9.3%	11.4%	0.162	9.5%	11.0%	0.325
Cholesterol		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[b]	--	O = 197.7	O = 194.3	0.053	O = 197.8	O = 194.3	0.041
(discrete)	High	13.5%	10.2%	0.045	14.3%	9.1%	<0.001
HDL Cholesterol		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	O = 43.59	O = 46.20	<0.001	O = 43.80	O = 45.68	<0.001
(discrete)	Low	17.8%	13.5%	0.017	18.1%	13.2%	0.005
Cholesterol-HDL Ratio		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	O = 4.49	O = 4.17	<0.001	O = 4.48	O = 4.22	<0.001
(discrete)	High	34.7%	27.3%	0.001	35.0%	27.2%	<0.001
Triglycerides		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	O = 139.9	O = 123.9	<0.001	O = 136.9	O = 129.3	0.021
(discrete)	High	13.3%	7.5%	<0.001	12.5%	9.2%	0.032
Creatine Phosphokinase		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	O = 107.7	O = 105.2	0.420	O = 107.9	O = 105.0	0.340
(discrete)	High	9.7%	10.5%	0.614	10.1%	9.7%	0.836
Serum Amylase		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	O = 54.93	O = 55.21	0.779	O = 55.10	O = 54.91	0.852
(discrete)	High	3.4%	2.6%	0.435	3.2%	3.0%	0.945
Antibodies for Hepatitis A		(n=1,257)	(n=690)		(n=1,215)	(n=732)	
	Yes	33.9%	33.6%	0.945	33.7%	33.9%	0.991
Serological Evidence of Prior Hepatitis B Infection	Yes	(n=1,259) 9.8%	(n=692) 8.1%	0.252	(n=1,217) 9.7%	(n=734) 8.3%	0.344
Antibodies for Hepatitis C		(n=1,259)	(n=692)		(n=1,217)	(n=734)	
	Yes	1.4%	0.9%	0.388	1.6%	0.5%	0.055
Stool Hemoccult		(n=1,159)	(n=641)		(n=1,120)	(n=680)	
	Yes	1.6%	1.3%	0.652	1.9%	0.9%	0.139
Protein Profile: Prealbumin		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[b]	--	O = 28.94	O = 28.75	0.490	O = 28.84	O = 28.93	0.751
(discrete)	Low	1.6%	1.6%	0.999	1.4%	1.9%	0.516

Table F-5. Dependent Variable-covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Cumulative Degreasing Chemical Exposure			Cumulative Industrial Chemical Exposure		
		Yes	No	p-Value	Yes	No	p-Value
Protein Profile: Albumin		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)	--	Ō = 4,189.4	Ō = 4,183.6	0.659	Ō = 4,188.1	Ō = 4,186.1	0.880
(discrete)	Low	0.7%	0.4%	0.793	0.6%	0.6%	0.999
Protein Profile: α-1-Acid Glycoprotein		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	Ō = 79.03	Ō = 76.89	0.017	Ō = 78.91	Ō = 77.20	0.052
(discrete)	High	5.3%	5.3%	0.999	5.1%	5.5%	0.802
Protein Profile: α-1-Antitrypsin		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[b]	--	Ō = 142.1	Ō = 138.8	0.007	Ō = 142.2	Ō = 138.8	0.006
(discrete)	Low	1.4%	1.6%	0.045	1.2%	1.9%	0.003
	Normal	86.8%	90.2%		86.6%	90.4%	
	High	11.8%	8.2%		12.2%	7.7%	
Protein Profile: α-2-Macroglobulin		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	Ō = 186.3	Ō = 185.4	0.738	Ō = 185.1	Ō = 187.3	0.428
(discrete)	High	14.2%	13.5%	0.693	13.6%	14.5%	0.601
Protein Profile: Apolipoprotein B		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[b]	--	Ō = 104.1	Ō = 100.2	<0.001	Ō = 103.9	Ō = 100.7	0.005
(discrete)	High	1.9%	1.6%	0.733	2.0%	1.5%	0.533
Protein Profile: C3 Complement		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[b]	--	Ō = 121.6	Ō = 115.7	<0.001	Ō = 120.9	Ō = 117.1	<0.001
(discrete)	Low	1.1%	2.6%	0.014	1.2%	2.3%	0.077
Protein Profile: C4 Complement		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[b]	--	Ō = 22.87	Ō = 22.14	0.007	Ō = 22.89	Ō = 22.16	0.007
(discrete)	Low	7.3%	8.5%	0.388	7.8%	7.5%	0.911
Protein Profile: Haptoglobin		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[b]	--	Ō = 125.1	Ō = 117.0	0.005	Ō = 124.2	Ō = 118.9	0.062
(discrete)	High	14.1%	9.8%	0.009	13.3%	11.3%	0.206
Protein Profile: Transferrin		(n=1,238)	(n=684)		(n=1,193)	(n=729)	
(continuous)[a]	--	Ō = 256.4	Ō = 251.1	0.006	Ō = 255.5	Ō = 252.9	0.164
(discrete)	Low	5.6%	6.6%	0.428	5.5%	6.6%	0.397
Prothrombin Time		(n=946)	(n=520)		(n=922)	(n=544)	
(continuous)[a]	--	Ō = 10.71	Ō = 10.74	0.167	Ō = 10.69	Ō = 10.77	0.003
(discrete)	High	0.9%	1.0%	0.999	0.8%	1.1%	0.697

Dependent Variable	Level	Body Mass Index (kg/m^2)			Current Alcohol Use (drinks/day)		
		Not Obese (≤30)	Obese (>30)	p-Value	0-1	>1	p-Value
Uncharacterized Hepatitis		(n=1,251)	(n=687)				
	Yes	1.6%	1.5%	0.959	--	--	--
Jaundice (unspecified)		(n=1,225)	(n=676)				
	Yes	2.6%	2.2%	0.708	--	--	--
Chronic Liver Disease and Cirrhosis (alcohol-related)		(n=1,190)	(n=649)				
	Yes	4.0%	4.6%	0.633	--	--	--
Chronic Liver Disease and Cirrhosis (nonalcohol-related)		(n=1,261)	(n=689)				
	Yes	1.9%	4.4%	0.003	--	--	--
Liver Abscess and Sequelae of Chronic Liver Disease		(n=1,261)	(n=689)				
	Yes	0.4%	0.3%	0.999	--	--	--
Enlarged Liver (hepatomegaly)		(n=1,260)	(n=688)				
	Yes	3.3%	4.4%	0.306	--	--	--
Other Disorders of the Liver		(n=1,249)	(n=689)				
	Yes	43.7%	50.2%	0.007	--	--	--
Current Hepatomegaly		(n=1,239)	(n=686)				
	Yes	0.8%	2.2%	0.019	--	--	--
AST		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = 0.059		0.009	r = 0.108		<0.001
(discrete)	High	6.9%	9.2%	0.077	6.9%	12.5%	0.001
ALT		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = 0.173		<0.001	r = 0.049		0.032
(discrete)	High	5.5%	10.8%	<0.001	7.4%	7.3%	0.999
GGT		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = 0.112		<0.001	r = 0.225		<0.001
(discrete)	High	9.9%	12.0%	0.165	8.8%	20.9%	<0.001
Alkaline Phosphatase		(n=1,238)	(n=683)				
(continuous)[a]	--	r = -0.015		0.523	--		--
(discrete)	High	7.2%	6.4%	0.601	--	--	--
Total Bilirubin		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = -0.016		0.487	r = 0.127		<0.001
(discrete)	High	6.7%	6.3%	0.803	5.8%	10.8%	0.003
Direct Bilirubin		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
	High	0.6%	0.9%	0.610	0.4%	2.1%	0.006
LDH		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = 0.165		<0.001	r = -0.043		0.059
(discrete)	High	8.2%	13.3%	<0.001	10.4%	8.0%	0.267
Cholesterol		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[b]	--	r = -0.106		<0.001	r = 0.103		<0.001
(discrete)	High	12.8%	11.4%	0.404	11.9%	15.0%	0.169

Dependent Variable	Level	Body Mass Index (kg/m^2)			Current Alcohol Use (drinks/day)		
		Not Obese (≤30)	Obese (>30)	p-Value	0-1	>1	p-Value
HDL Cholesterol		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = -0.320		<0.001	r = 0.291		<0.001
(discrete)	Low	12.2%	23.6%	<0.001	18.6%	2.8%	<0.001
Cholesterol-HDL Ratio		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = 0.226		<0.001	r = -0.202		<0.001
(discrete)	High	27.7%	40.0%	<0.001	34.2%	19.5%	<0.001
Triglycerides		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = 0.237		<0.001	r = -0.025		0.276
(discrete)	High	9.1%	15.2%	<0.001	11.0%	12.5%	0.515
Creatine Phosphokinase		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = 0.226		<0.001	r = -0.047		0.039
(discrete)	High	8.6%	12.6%	0.006	10.5%	7.0%	0.080
Serum Amylase		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = -0.187		<0.001	r = -0.045		0.049
(discrete)	High	3.8%	1.9%	0.032	3.3%	2.4%	0.589
Antibodies for Hepatitis A		(n=1,257)	(n=689)		(n=1,655)	(n=290)	
	Yes	34.5%	32.5%	0.416	34.6%	29.0%	0.073
Serological Evidence of Prior Hepatitis B Infection		(n=1,261)	(n=689)		(n=1,657)	(n=292)	
	Yes	8.5%	10.5%	0.176	9.6%	6.9%	0.165
Antibodies for Hepatitis C		(n=1,261)	(n=689)		(n=1,657)	(n=292)	
	Yes	1.7%	0.4%	0.032	1.2%	1.4%	0.999
Stool Hemoccult		(n=1,156)	(n=643)		(n=1,528)	(n=270)	
	Yes	1.3%	1.9%	0.454	1.6%	0.7%	0.437
Protein Profile: Prealbumin		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[b]	--	r = -0.097		<0.001	r = 0.135		<0.001
(discrete)	Low	1.8%	1.3%	0.565	1.5%	2.1%	0.660
Protein Profile: Albumin		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)	--	r = -0.077		<0.001	r = -0.019		0.396
(discrete)	Low	0.7%	0.3%	0.373	0.6%	0.7%	0.999
Protein Profile: α-1-Acid Glycoprotein		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = 0.024		0.284	r = 0.053		0.019
(discrete)	High	5.7%	4.4%	0.248	5.0%	7.0%	0.207
Protein Profile: α-1-Antitrypsin		(n=1,238)	(n=683)				
(continuous)[b]	--	r = -0.053		0.019	--		--
(discrete)	Low	1.7%	1.0%	<0.001	--	--	--
	Normal	85.9%	92.0%		--	--	
	High	12.4%	7.0%		--	--	
Protein Profile: α-2-Macroglobulin		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = -0.001		0.982	r = -0.077		<0.001
(discrete)	High	11.6%	18.2%	<0.001	14.6%	9.8%	0.035

Dependent Variable	Level	Body Mass Index (kg/m^2)			Current Alcohol Use (drinks/day)		
		Not Obese (≤30)	Obese (>30)	p-Value	0-1	>1	p-Value
Protein Profile: Apolipoprotein B		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[b]	--	r = -0.005		0.827	r = 0.011		0.643
(discrete)	High	1.4%	2.6%	0.072	1.7%	2.8%	0.278
Protein Profile: C3 Complement		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[b]	--	r = 0.348		<0.001	r = -0.153		<0.001
(discrete)	Low	2.3%	0.4%	0.004	1.5%	2.4%	0.343
Protein Profile: C4 Complement		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[b]	--	r = 0.094		<0.001	r = -0.044		0.054
(discrete)	Low	8.1%	7.0%	0.461	7.5%	9.1%	0.418
Protein Profile: Haptoglobin		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[b]	--	r = 0.049		0.030	r = 0.026		0.248
(discrete)	High	13.3%	11.1%	0.186	12.8%	11.2%	0.496
Protein Profile: Transferrin		(n=1,238)	(n=683)		(n=1,633)	(n=287)	
(continuous)[a]	--	r = 0.072		0.002	r = 0.031		0.177
(discrete)	Low	6.5%	5.0%	0.224	5.8%	6.6%	0.693
Prothrombin Time		(n=983)	(n=483)		(n=1,249)	(n=216)	
(continuous)[a]	--	r = -0.0003		0.992	r = -0.021		0.412
(discrete)	High	0.6%	1.5%	0.189	1.0%	0.5%	0.743

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	>0-40	>40	p-Value
Uncharacterized Hepatitis		(n=107)	(n=1,226)	(n=597)	
	Yes	3.7%	2.0%	0.3%	0.005
Jaundice (unspecified)		(n=106)	(n=1,198)	(n=590)	
	Yes	2.8%	2.8%	1.9%	0.509
Chronic Liver Disease and Cirrhosis (alcohol-related)			(n=1,233)	(n=598)	
	Yes	--	1.2%	10.5%	<0.001
Chronic Liver Disease and Cirrhosis (nonalcohol-related)		(n=107)	(n=1,234)	(n=601)	
	Yes	2.8%	3.0%	2.3%	0.716
Liver Abscess and Sequelae of Chronic Liver Disease		(n=107)	(n=1,234)	(n=601)	
	Yes	0.0%	0.3%	0.5%	0.686
Enlarged Liver (hepatomegaly)		(n=107)	(n=1,233)	(n=600)	
	Yes	0.9%	2.8%	6.0%	0.001
Other Disorders of the Liver		(n=107)	(n=1,225)	(n=598)	
	Yes	47.7%	44.3%	49.2%	0.142
AST		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = 0.074		0.001
(discrete)	High	7.5%	7.6%	8.0%	0.948
ALT		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = -0.013		0.578
(discrete)	High	10.3%	7.6%	6.5%	0.355

Table F-5. Dependent Variable-covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	**>0-40**	**>40**	**p-Value**
GGT		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = 0.153		<0.001
(discrete)	High	9.4%	8.4%	15.6%	<0.001
Total Bilirubin		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = 0.032		0.156
(discrete)	High	2.8%	6.6%	7.2%	0.243
Direct Bilirubin		(n=107)	(n=1,221)	(n=585)	
	High	0.0%	0.4%	1.4%	0.046
LDH		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = -0.031		0.181
(discrete)	High	11.2%	10.2%	9.4%	0.787
Cholesterol		(n=107)	(n=1,221)	(n=585)	
(continuous)[b]	--		r = 0.049		0.032
(discrete)	High	10.3%	11.6%	14.4%	0.189
HDL Cholesterol		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = 0.145		<0.001
(discrete)	Low	29.0%	18.4%	9.2%	<0.001
Cholesterol-HDL Ratio		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = -0.103		<0.001
(discrete)	High	42.1%	34.2%	25.8%	<0.001
Triglycerides		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = 0.007		0.768
(discrete)	High	9.4%	11.5%	11.1%	0.796
Creatine Phosphokinase		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = -0.074		0.001
(discrete)	High	9.4%	11.0%	8.0%	0.145
Serum Amylase		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = -0.041		0.073
(discrete)	High	3.7%	3.0%	3.3%	0.869
Antibodies for Hepatitis A		(n=107)	(n=1,232)	(n=599)	
	Yes	45.8%	32.2%	34.6%	0.015
Serological Evidence of Prior Hepatitis B Infection		(n=107)	(n=1,234)	(n=601)	
	Yes	4.7%	8.4%	11.8%	0.014
Antibodies for Hepatitis C		(n=107)	(n=1,234)	(n=601)	
	Yes	0.0%	0.8%	2.3%	0.011
Stool Hemoccult		(n=100)	(n=1,150)	(n=541)	
	Yes	1.0%	1.7%	1.1%	0.635
Protein Profile: Prealbumin		(n=107)	(n=1,221)	(n=585)	
(continuous)[b]	--		r = 0.049		0.033
(discrete)	Low	0.9%	1.4%	2.2%	0.360

Table F-5. Dependent Variable-covariate Associations for the Gastrointestinal Assessment (Continued)

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	>0-40	>40	p-Value
Protein Profile: Albumin		(n=107)	(n=1,221)	(n=585)	
(continuous)	--		r = 0.004		0.877
(discrete)	Low	1.9%	0.5%	0.5%	0.190
Protein Profile: α-1-Acid Glycoprotein		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = 0.101		<0.001
(discrete)	High	0.9%	4.9%	6.7%	0.036
Protein Profile: α-1-Antitrypsin		(n=107)	(n=1,221)	(n=585)	
(continuous)[b]	--		r = 0.082		<0.001
(discrete)	Low	0.0%	1.6%	1.5%	0.005
	Normal	91.6%	89.5%	84.1%	
	High	8.4%	8.9%	14.4%	
Protein Profile: α-2-Macroglobulin		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = 0.023		0.323
(discrete)	High	27.1%	12.9%	13.7%	<0.001
Protein Profile: Apolipoprotein B		(n=107)	(n=1,221)	(n=585)	
(continuous)[b]	--		r = -0.002		0.936
(discrete)	High	1.9%	1.6%	2.2%	0.686
Protein Profile: C3 Complement		(n=107)	(n=1,221)	(n=585)	
(continuous)[b]	--		r = -0.036		0.115
(discrete)	Low	0.0%	1.5%	2.2%	0.196
Protein Profile: C4 Complement		(n=107)	(n=1,221)	(n=585)	
(continuous)[b]	--		r = 0.013		0.560
(discrete)	Low	7.5%	7.7%	7.9%	0.987
Protein Profile: Haptoglobin		(n=107)	(n=1,221)	(n=585)	
(continuous)[b]	--		r = 0.091		<0.001
(discrete)	High	9.4%	12.0%	14.2%	0.256
Protein Profile: Transferrin		(n=107)	(n=1,221)	(n=585)	
(continuous)[a]	--		r = 0.020		0.384
(discrete)	Low	7.5%	5.5%	6.7%	0.485
Prothrombin Time		(n=79)	(n=945)	(n=437)	
(continuous)[a]	--		r = 0.008		0.757
(discrete)	High	1.3%	0.9%	0.9%	0.928

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				
		Never	Former	>0-20	>20	p-Value
AST		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--		r = -0.097			<0.001
(discrete)	High	9.2%	7.1%	6.0%	8.8%	0.343
ALT		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--		r = -0.104			<0.001
(discrete)	High	9.4%	6.9%	4.5%	7.0%	0.094

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				p-Value
		Never	Former	>0-20	>20	
GGT		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--	r = 0.045				0.048
(discrete)	High	10.1%	10.4%	12.4%	14.0%	0.649
Alkaline Phosphatase		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--	r = 0.108				<0.001
(discrete)	High	5.5%	6.3%	14.9%	5.3%	<0.001
Total Bilirubin		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--	r = -0.085				<0.001
(discrete)	High	7.5%	6.3%	6.5%	1.8%	0.361
Direct Bilirubin		(n=597)	(n=1,065)	(n=201)	(n=57)	
	High	0.7%	0.4%	2.5%	0.0%	0.009
LDH		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--	r = -0.079				<0.001
(discrete)	High	8.0%	11.9%	7.0%	5.3%	0.015
Cholesterol		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[b]	--	r = 0.014				0.550
(discrete)	High	13.1%	11.8%	12.4%	14.0%	0.874
HDL Cholesterol		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--	r = -0.043				0.060
(discrete)	Low	15.1%	16.1%	17.9%	24.6%	0.268
Cholesterol-HDL Ratio		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--	r = 0.049				0.032
(discrete)	High	31.2%	31.0%	34.3%	52.6%	0.006
Triglycerides		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--	r = 0.033				0.143
(discrete)	High	9.2%	12.0%	12.4%	14.0%	0.279
Creatine Phosphokinase		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--	r = -0.098				<0.001
(discrete)	High	8.9%	11.6%	6.0%	7.0%	0.049
Serum Amylase		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--	r = -0.039				0.086
(discrete)	High	2.2%	3.5%	4.0%	3.5%	0.438
Antibodies for Hepatitis A		(n=599)	(n=1,074)	(n=214)	(n=58)	
	Yes	35.1%	33.9%	29.9%	31.0%	0.557
Serological Evidence of Prior Hepatitis B Infection		(n=601)	(n=1,076)	(n=214)	(n=58)	
	Yes	5.8%	9.6%	15.0%	15.5%	<0.001
Antibodies for Hepatitis C		(n=601)	(n=1,076)	(n=214)	(n=58)	
	Yes	0.5%	1.0%	4.7%	0.0%	<0.001
Stool Hemoccult		(n=567)	(n=995)	(n=182)	(n=54)	
	Yes	1.2%	1.9%	0.0%	0.0%	0.162

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				p-Value
		Never	Former	>0-20	>20	
Protein Profile: Prealbumin		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[b]	--	r = -0.060				0.008
(discrete)	Low	1.5%	1.2%	3.5%	3.5%	0.079
Protein Profile: Albumin		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)	--	r = -0.062				0.007
(discrete)	Low	0.7%	0.6%	0.5%	0.0%	0.930
Protein Profile: α-1-Acid Glycoprotein		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--	r = 0.163				<0.001
(discrete)	High	2.4%	6.0%	8.5%	10.5%	<0.001
Protein Profile: α-1-Antitrypsin		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[b]	--	r = 0.235				<0.001
(discrete)	Low	1.5%	1.8%	0.0%	0.0%	<0.001
	Normal	94.0%	88.9%	71.1%	68.4%	
	High	4.5%	9.3%	28.9%	31.6%	
Protein Profile: α-2-Macroglobulin		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--	r = 0.041				0.073
(discrete)	High	11.9%	14.7%	15.4%	14.0%	0.387
Protein Profile: Apolipoprotein B		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[b]	--	r = 0.036				0.113
(discrete)	High	1.8%	2.0%	1.5%	0.0%	0.726
Protein Profile: C3 Complement		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[b]	--	r = -0.017				0.468
(discrete)	Low	1.2%	1.8%	2.0%	1.8%	0.774
Protein Profile: C4 Complement		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[b]	--	r = -0.007				0.758
(discrete)	Low	9.4%	6.5%	10.0%	5.3%	0.089
Protein Profile: Haptoglobin		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[b]	--	r = 0.199				<0.001
(discrete)	High	6.4%	12.6%	23.4%	38.6%	<0.001
Protein Profile: Transferrin		(n=597)	(n=1,065)	(n=201)	(n=57)	
(continuous)[a]	--	r = 0.022				0.338
(discrete)	Low	6.7%	6.0%	4.5%	1.8%	0.364
Prothrombin Time		(n=473)	(n=787)	(n=160)	(n=45)	
(continuous)[a]	--	r = -0.074				0.005
(discrete)	High	0.4%	1.1%	1.3%	0.0%	0.496

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			p-Value
		0	>0-10	>10	
Uncharacterized Hepatitis		(n=597)	(n=488)	(n=851)	
	Yes	2.0%	1.6%	1.2%	0.441
Jaundice (unspecified)		(n=587)	(n=475)	(n=837)	
	Yes	2.9%	2.5%	2.2%	0.670

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	**>0-10**	**>10**	**p-Value**
Chronic Liver Disease and Cirrhosis (alcohol-related)		(n=536)	(n=478)	(n=823)	
	Yes	3.4%	3.8%	5.1%	0.247
Chronic Liver Disease and Cirrhosis (nonalcohol-related)		(n=601)	(n=491)	(n=856)	
	Yes	3.0%	3.5%	2.2%	0.378
Liver Abscess and Sequelae of Chronic Liver Disease		(n=601)	(n=491)	(n=856)	
	Yes	0.5%	0.0%	0.5%	0.305
Enlarged Liver (hepatomegaly)		(n=600)	(n=491)	(n=855)	
	Yes	2.7%	3.7%	4.4%	0.209
Other Disorders of the Liver		(n=595)	(n=489)	(n=852)	
	Yes	43.5%	44.4%	48.6%	0.117

Dependent Variable	Level	Current Wine Consumption (drinks of wine/day)			Lifetime Wine History (drink-years)		
		0	**>0**	**p-Value**	**0**	**>0**	**p-Value**
Alkaline Phosphatase		(n=1,245)	(n=675)		(n=503)	(n=1,414)	
(continuous)[a]	--	r = -0.102		<0.001	r = -0.078		<0.001
(discrete)	High	7.9%	5.2%	0.034	8.8%	6.3%	0.079
Protein Profile: α-1-Antitrypsin		(n=1,245)	(n=675)				
(continuous)[b]	--	r = -0.080		<0.001	--		--
(discrete)	Low	1.0%	2.4%	<0.001	--	--	--
	Normal	86.1%	91.6%				
	High	12.9%	6.1%				

Dependent Variable	Level	Compliance to Dietary Restrictions		
		Yes	**No**	**p-Value**
Stool Hemoccult		(n=1,544)	(n=256)	
	Yes	1.6%	1.2%	0.850

[a]Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.

[b]Analysis performed on square root scale; means transformed from square root scale.

--: The covariate was not applicable for this dependent variable.

Note: Please see Section 13.1.3 and Table 13-1 for a further discussion of the dependent variables and covariates shown in this appendix.

Table F-6. Dependent Variable-covariate Associations for the Dermatology Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Acne (lifetime)		(n=890)	(n=1,061)		(n=125)	(n=1,826)	
	Yes	50.9%	37.0%	<0.001	40.8%	43.5%	0.614
Post-SEA Acne		(n=889)	(n=1,061)		(n=125)	(n=1,825)	
	Yes	30.8%	16.0%	<0.001	28.8%	22.4%	0.121
Post-SEA Acne (no pre-SEA acne)		(n=551)	(n=735)		(n=98)	(n=1,188)	
	Yes	20.5%	9.1%	<0.001	24.5%	13.1%	0.003
Post-SEA Acne (with pre-SEA acne)		(n=338)	(n=326)		(n=27)	(n=637)	
	Yes	47.6%	31.6%	<0.001	44.4%	39.6%	0.759
Location of Post-SEA Acne (excluding participants with pre-SEA acne)	Temples, Eyes, Ears	(n=113) 31.0%	(n=64) 26.6%	0.655	(n=24) 37.5%	(n=153) 28.1%	0.485
Location of Post-SEA Acne (all post-SEA occurrences)	Temples, Eyes, Ears	(n=272) 33.8%	(n=166) 38.6%	0.368	(n=36) 38.9%	(n=402) 35.3%	0.805
Duration of Post-SEA Acne (excluding participants with pre-SEA acne)[a]	--	n=174 r = -0.098		0.199	(n=24) Õ = 51.37	(n=150) Õ = 61.58	0.515
Duration of Post-SEA Acne (all post-SEA occurrences)[a]	--	n=433 r = -0.023		0.627	(n=36) Õ = 87.31	(n=397) Õ = 134.95	0.042
Acneiform Lesions		(n=890)	(n=1,061)		(n=125)	(n=1,826)	
	Yes	6.7%	4.1%	0.011	3.2%	5.4%	0.386
Acneiform Scars		(n=890)	(n=1,061)		(n=125)	(n=1,826)	
	Yes	8.1%	4.9%	0.005	7.2%	6.3%	0.833
Comedones		(n=890)	(n=1,061)		(n=125)	(n=1,826)	
	Yes	4.7%	7.4%	0.021	4.8%	6.2%	0.648
Depigmentation		(n=890)	(n=1,061)		(n=125)	(n=1,826)	
	Yes	2.5%	2.9%	0.639	5.6%	2.5%	0.078
Hyperpigmentation		(n=890)	(n=1,061)		(n=125)	(n=1,826)	
	Yes	6.0%	8.9%	0.020	17.6%	6.9%	<0.001
Inclusion Cysts		(n=890)	(n=1,061)		(n=125)	(n=1,826)	
	Yes	11.7%	12.1%	0.852	7.2%	12.2%	0.126
Dermatology Index		(n=890)	(n=1,061)		(n=125)	(n=1,826)	
	Abnormal	24.4%	23.0%	0.507	16.0%	24.2%	0.049

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Acne (lifetime)		(n=769)	(n=318)	(n=864)	
	Yes	41.9%	41.5%	45.4%	0.278
Post-SEA Acne		(n=769)	(n=318)	(n=863)	
	Yes	16.5%	21.4%	28.9%	<0.001

Table F-6. Dependent Variable-covariate Associations for the Dermatology Assessment (Continued)

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Post-SEA Acne (no pre-SEA acne)		(n=490)	(n=214)	(n=582)	
	Yes	8.8%	13.1%	18.7%	<0.001
Post-SEA Acne (with pre-SEA acne)		(n=279)	(n=104)	(n=281)	
	Yes	30.1%	38.5%	49.8%	<0.001
Location of Post-SEA Acne (excluding participants with pre-SEA acne)	Temples, Eyes, Ears	(n=43) 16.3%	(n=26) 38.5%	(n=108) 32.4%	0.079
Location of Post-SEA Acne (all post-SEA occurrences)	Temples, Eyes, Ears	(n=126) 31.0%	(n=66) 43.9%	(n=246) 35.8%	0.203
Duration of Post-SEA Acne (excluding participants with pre-SEA acne)[a]	--	(n=41) Õ = 39.08	(n=26) Õ = 70.21	(n=107) Õ = 66.87	0.065
Duration of Post-SEA Acne (all post-SEA occurrences)[a]	--	(n=124) Õ = 131.60	(n=66) Õ = 136.83	(n=243) Õ = 128.42	0.917
Acneiform Lesions		(n=769)	(n=318)	(n=864)	
	Yes	3.3%	5.0%	7.2%	0.002
Acneiform Scars		(n=769)	(n=318)	(n=864)	
	Yes	4.8%	8.2%	7.1%	0.062
Comedones		(n=769)	(n=318)	(n=864)	
	Yes	4.8%	10.1%	5.9%	0.004
Depigmentation		(n=769)	(n=318)	(n=864)	
	Yes	2.1%	3.5%	3.0%	0.346
Hyperpigmentation		(n=769)	(n=318)	(n=864)	
	Yes	6.5%	8.5%	8.1%	0.369
Inclusion Cysts		(n=769)	(n=318)	(n=864)	
	Yes	10.7%	14.2%	12.2%	0.258
Dermatology Index		(n=769)	(n=318)	(n=864)	
	Abnormal	19.3%	28.0%	25.9%	<0.001

Dependent Variable	Level	Presence of Pre-SEA Acne		
		Yes	No	p-Value
Acneiform Lesions		(n=664)	(n=1,286)	
	Yes	7.8%	4.0%	<0.001
Acneiform Scars		(n=664)	(n=1,286)	
	Yes	12.1%	3.4%	<0.001
Comedones		(n=664)	(n=1,286)	
	Yes	7.8%	5.3%	0.034
Depigmentation		(n=664)	(n=1,286)	
	Yes	2.6%	2.8%	0.872
Hyperpigmentation		(n=664)	(n=1,286)	
	Yes	6.9%	7.9%	0.520

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Table F-6. Dependent Variable-covariate Associations for the Dermatology Assessment (Continued)

| Dependent Variable | Level | Presence of Pre-SEA Acne | | |
		Yes	No	p-Value
Inclusion Cysts		(n=664)	(n=1,286)	
	Yes	14.2%	10.7%	0.032
Dermatology Index		(n=664)	(n=1,286)	
	Abnormal	31.2%	19.8%	<0.001

[a]Analysis performed on square root scale; means transformed from square root scale.

Note: Please see Section 14.1.3 and Table 14-1 for a further discussion of the dependent variables and covariates shown in this appendix.

Table F-7. Dependent Variable-covariate Associations for the Cardiovascular Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Essential Hypertension		(n=877)	(n=1,028)		(n=120)	(n=1,785)	
	Yes	44.8%	64.5%	<0.001	62.5%	55.0%	0.130
Heart Disease (Excluding		(n=883)	(n=1,040)		(n=121)	(n=1,802)	
Essential Hypertension)	Yes	76.4%	87.1%	<0.001	85.1%	82.0%	0.458
Myocardial Infarction		(n=883)	(n=1,040)		(n=121)	(n=1,802)	
	Yes	5.7%	15.3%	<0.001	8.3%	11.0%	0.424
Stroke or Transient Ischemic		(n=883)	(n=1,040)		(n=121)	(n=1,802)	
Attack	Yes	1.4%	5.1%	<0.001	3.3%	3.4%	0.999
Systolic Blood Pressure (mm Hg)		(n=883)	(n=1,039)		(n=121)	(n=1,801)	
(continuous)	--	r = 0.080		<0.001	Ō = 129.7	Ō = 128.6	0.491
(discrete)	High	20.7%	28.2%	<0.001	27.3%	24.6%	0.582
Diastolic Blood Pressure (mm Hg)		(n=883)	(n=1,039)		(n=121)	(n=1,801)	
(continuous)	--	r = -0.277		<0.001	Ō = 77.22	Ō = 74.75	0.007
(discrete)	High	6.1%	4.1%	0.062	9.1%	4.8%	0.060
Heart Sounds		(n=883)	(n=1,039)		(n=121)	(n=1,801)	
	Abnormal	3.7%	8.6%	<0.001	5.8%	6.4%	0.945
Overall Electrocardiograph (ECG)		(n=883)	(n=1,039)		(n=121)	(n=1,801)	
	Abnormal	22.3%	47.0%	<0.001	40.5%	35.3%	0.292
ECG: RBBB		(n=883)	(n=1,039)		(n=121)	(n=1,801)	
	Yes	1.5%	5.9%	<0.001	1.7%	4.0%	0.292
ECG: LBBB		(n=883)	(n=1,039)		(n=121)	(n=1,801)	
	Yes	0.8%	1.6%	0.146	0.0%	1.3%	0.393
ECG: Nonspecific ST- and		(n=883)	(n=1,039)		(n=121)	(n=1,801)	
T-wave Changes	Yes	16.9%	28.9%	<0.001	33.1%	22.7%	0.013
ECG: Bradycardia		(n=883)	(n=1,039)		(n=121)	(n=1,801)	
	Yes	3.7%	6.0%	0.032	2.5%	5.1%	0.283
ECG: Tachycardia		(n=883)	(n=1,039)		(n=121)	(n=1,801)	
	Yes	0.5%	0.6%	0.952	0.0%	0.6%	0.866
ECG: Arrhythmia		(n=883)	(n=1,039)		(n=121)	(n=1,801)	
	Yes	5.4%	14.4%	<0.001	5.0%	10.7%	0.065
ECG: Evidence of Prior		(n=883)	(n=1,039)		(n=121)	(n=1,801)	
Myocardial Infarction	Yes	1.9%	7.5%	<0.001	2.5%	5.1%	0.283
Funduscopic Examination		(n=845)	(n=916)		(n=107)	(n=1,654)	
	Abnormal	6.3%	14.6%	<0.001	14.0%	10.4%	0.310
Carotid Bruits		(n=883)	(n=1,039)		(n=121)	(n=1,801)	
	Present	0.9%	3.5%	<0.001	2.5%	2.3%	0.999
Radial Pulses		(n=881)	(n=1,032)		(n=120)	(n=1,793)	
	Abnormal	8.7%	5.1%	0.002	4.2%	7.0%	0.320
Femoral Pulses		(n=883)	(n=1,040)		(n=121)	(n=1,802)	
	Abnormal	0.7%	1.5%	0.121	2.5%	1.1%	0.325

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Popliteal Pulses		(n=881)	(n=1,039)		(n=121)	(n=1,799)	
	Abnormal	1.0%	3.8%	<0.001	4.1%	2.4%	0.375
Dorsalis Pedis Pulses		(n=881)	(n=1,036)		(n=120)	(n=1,797)	
	Abnormal	4.4%	11.4%	<0.001	12.5%	7.9%	0.108
Posterior Tibial Pulses		(n=882)	(n=1,036)		(n=120)	(n=1,798)	
	Abnormal	2.5%	7.6%	<0.001	5.8%	5.2%	0.939
Leg Pulses		(n=879)	(n=1,036)		(n=121)	(n=1,794)	
	Abnormal	5.2%	12.9%	<0.001	13.2%	9.1%	0.184
Peripheral Pulses		(n=877)	(n=1,029)		(n=120)	(n=1,786)	
	Abnormal	13.0%	16.9%	0.021	15.8%	15.1%	0.923
Resting Pressure Index		(n=876)	(n=1,025)		(n=119)	(n=1,782)	
(continuous)	--	r = -0.153		<0.001	Ō = 1.214	Ō = 1.255	0.004
(discrete)	Low	1.5%	5.8%	<0.001	5.0%	3.7%	0.622
Hyperemic Pressure Index (1 minute post-exercise)		(n=859)	(n=989)		(n=116)	(n=1,732)	
(continuous)	--	r = -0.104		<0.001	Ō = 1.126	Ō = 1.176	0.004
(discrete)	Low	6.5%	12.0%	<0.001	12.1%	9.3%	0.410
Hyperemic Pressure Index (2 minutes post-exercise)		(n=859)	(n=991)		(n=116)	(n=1,734)	
(continuous)	--	r = -0.144		<0.001	Ō = 1.191	Ō = 1.230	0.014
(discrete)	Low	2.6%	7.8%	<0.001	7.8%	5.2%	0.329
Intermittent Claudication and Vascular Insufficiency Index	Abnormal	(n=882) 1.7%	(n=1,039) 4.2%	0.002	(n=121) 4.1%	(n=1,800) 3.0%	0.670

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Essential Hypertension		(n=747)	(n=313)	(n=845)	
	Yes	55.2%	60.1%	54.0%	0.176
Heart Disease (Excluding Essential Hypertension)		(n=755)	(n=315)	(n=853)	
	Yes	84.9%	85.4%	78.7%	0.001
Myocardial Infarction		(n=755)	(n=315)	(n=853)	
	Yes	10.7%	13.3%	10.1%	0.282
Stroke or Transient Ischemic Attack		(n=755)	(n=315)	(n=853)	
	Yes	3.8%	4.1%	2.7%	0.325
Systolic Blood Pressure (mm Hg)		(n=754)	(n=315)	(n=853)	
(continuous)	--	Ō = 129.4	Ō = 130.1	Ō = 127.6	0.032
(discrete)	High	27.3%	26.0%	22.0%	0.043
Diastolic Blood Pressure (mm Hg)		(n=754)	(n=315)	(n=853)	
(continuous)	--	Ō = 73.57	Ō = 74.76	Ō = 76.14	<0.001
(discrete)	High	4.0%	5.4%	5.9%	0.217

Dependent Variable	Level	Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
				Military Occupation	
Heart Sounds		(n=754)	(n=315)	(n=853)	
	Abnormal	7.7%	5.7%	5.4%	0.149
Overall Electrocardiograph (ECG)		(n=754)	(n=315)	(n=853)	
	Abnormal	40.1%	41.9%	29.4%	<0.001
ECG: RBBB		(n=754)	(n=315)	(n=853)	
	Yes	4.0%	6.7%	2.7%	0.007
ECG: LBBB		(n=754)	(n=315)	(n=853)	
	Yes	1.5%	1.0%	1.2%	0.765
ECG: Non-specific ST- and T-wave Changes		(n=754)	(n=315)	(n=853)	
	Yes	24.1%	29.2%	20.5%	0.006
ECG: Bradycardia		(n=754)	(n=315)	(n=853)	
	Yes	6.6%	3.8%	3.9%	0.023
ECG: Tachycardia		(n=754)	(n=315)	(n=853)	
	Yes	0.1%	0.3%	0.9%	0.070
ECG: Arrhythmia		(n=754)	(n=315)	(n=853)	
	Yes	13.1%	10.2%	7.9%	0.002
ECG: Evidence of Prior Myocardial Infarction		(n=754)	(n=315)	(n=853)	
	Yes	6.0%	7.0%	3.3%	0.009
Funduscopic Examination		(n=683)	(n=288)	(n=790)	
	Abnormal	8.9%	12.9%	11.3%	0.142
Carotid Bruits		(n=754)	(n=315)	(n=853)	
	Present	3.1%	2.2%	1.6%	0.169
Radial Pulses		(n=749)	(n=313)	(n=851)	
	Abnormal	7.2%	5.1%	7.1%	0.429
Femoral Pulses		(n=755)	(n=315)	(n=853)	
	Abnormal	1.2%	1.9%	0.8%	0.299
Popliteal Pulses		(n=754)	(n=314)	(n=852)	
	Abnormal	2.9%	3.8%	1.6%	0.069
Dorsalis Pedis Pulses		(n=751)	(n=314)	(n=852)	
	Abnormal	9.2%	8.9%	7.0%	0.258
Posterior Tibial Pulses		(n=753)	(n=312)	(n=853)	
	Abnormal	5.6%	6.1%	4.7%	0.566
Leg Pulses		(n=751)	(n=313)	(n=851)	
	Abnormal	10.5%	10.2%	8.1%	0.221
Peripheral Pulses		(n=746)	(n=311)	(n=849)	
	Abnormal	16.6%	14.8%	13.9%	0.313
Resting Pressure Index		(n=748)	(n=313)	(n=840)	
(continuous)	--	$\bar{O}$ = 1.268	$\bar{O}$ = 1.230	$\bar{O}$ = 1.246	<0.001
(discrete)	Low	4.6%	4.8%	2.7%	0.101

Dependent Variable	Level	Military Occupation			
		Officer	**Enlisted Flyer**	**Enlisted Groundcrew**	**p-Value**
Hyperemic Pressure Index (1 minute post-exercise)		(n=729)	(n=300)	(n=819)	
(continuous)	--	O = 1.203	O = 1.130	O = 1.163	<0.001
(discrete)	Low	7.7%	15.0%	9.0%	0.001
Hyperemic Pressure Index (2 minutes post-exercise)		(n=731)	(n=300)	(n=819)	
(continuous)	--	O = 1.252	O = 1.195	O = 1.218	<0.001
(discrete)	Low	5.3%	7.0%	4.8%	0.338
Intermittent Claudication and Vascular Insufficiency Index	Abnormal	(n=755) 2.8%	(n=315) 2.9%	(n=851) 3.4%	0.746

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	**>0-10**	**>10**	**p-Value**
Essential Hypertension		(n=591)	(n=480)	(n=831)	
	Yes	52.0%	52.9%	59.3%	0.010
Heart Disease (Excluding Essential Hypertension)		(n=595)	(n=486)	(n=839)	
	Yes	81.9%	80.7%	83.3%	0.461
Myocardial Infarction		(n=595)	(n=486)	(n=839)	
	Yes	6.4%	9.3%	14.9%	<0.001
Stroke or Transient Ischemic Attack		(n=595)	(n=486)	(n=839)	
	Yes	3.2%	1.9%	4.3%	0.057
Systolic Blood Pressure (mm Hg)		(n=595)	(n=486)	(n=838)	
(continuous)	--		r = 0.005		0.832
(discrete)	High	23.2%	25.3%	25.4%	0.590
Diastolic Blood Pressure (mm Hg)		(n=595)	(n=486)	(n=838)	
(continuous)	--		r = -0.101		<0.001
(discrete)	High	5.7%	6.0%	4.1%	0.210
Heart Sounds		(n=595)	(n=486)	(n=838)	
	Abnormal	6.1%	4.9%	7.3%	0.229
Overall Electrocardiograph (ECG)		(n=595)	(n=486)	(n=838)	
	Abnormal	32.6%	34.0%	38.8%	0.037
ECG: RBBB		(n=595)	(n=486)	(n=838)	
	Yes	3.4%	2.9%	4.8%	0.170
ECG: LBBB		(n=595)	(n=486)	(n=838)	
	Yes	1.0%	1.0%	1.6%	0.580
ECG: Nonspecific ST- and T-wave Changes		(n=595)	(n=486)	(n=838)	
	Yes	20.8%	23.5%	25.1%	0.177
ECG: Bradycardia		(n=595)	(n=486)	(n=838)	
	Yes	5.6%	5.6%	4.2%	0.388
ECG: Tachycardia		(n=595)	(n=486)	(n=838)	
	Yes	0.3%	0.2%	0.8%	0.232

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	**>0-10**	**>10**	**p-Value**
ECG: Arrhythmia		(n=595)	(n=486)	(n=838)	
	Yes	9.8%	10.7%	10.5%	0.854
ECG: Evidence of Prior Myocardial		(n=595)	(n=486)	(n=838)	
Infarction	Yes	3.2%	3.7%	6.8%	0.003
Funduscopic Examination		(n=549)	(n=448)	(n=761)	
	Abnormal	7.5%	11.2%	12.4%	0.016
Carotid Bruits		(n=595)	(n=486)	(n=838)	
	Present	1.2%	1.9%	3.2%	0.029
Radial Pulses		(n=590)	(n=483)	(n=837)	
	Abnormal	5.8%	7.3%	7.2%	0.513
Femoral Pulses		(n=595)	(n=486)	(n=839)	
	Abnormal	0.0%	1.4%	1.8%	0.006
Popliteal Pulses		(n=594)	(n=485)	(n=838)	
	Abnormal	0.5%	3.1%	3.5%	0.001
Dorsalis Pedis Pulses		(n=594)	(n=484)	(n=836)	
	Abnormal	4.0%	7.0%	11.7%	<0.001
Posterior Tibial Pulses		(n=594)	(n=485)	(n=836)	
	Abnormal	1.5%	5.0%	8.0%	<0.001
Leg Pulses		(n=593)	(n=485)	(n=834)	
	Abnormal	4.6%	8.3%	13.4%	<0.001
Peripheral Pulses		(n=588)	(n=482)	(n=833)	
	Abnormal	10.0%	14.3%	19.0%	<0.001
Resting Pressure Index		(n=589)	(n=479)	(n=830)	
(continuous)	--		r = -0.263		<0.001
(discrete)	Low	1.0%	3.1%	6.1%	<0.001
Hyperemic Pressure Index (1 minute post-exercise)		(n=577)	(n=466)	(n=802)	
(continuous)	--		r = -0.283		<0.001
(discrete)	Low	2.1%	7.3%	16.0%	<0.001
Hyperemic Pressure Index (2 minutes post-exercise)		(n=578)	(n=467)	(n=802)	
(continuous)	--		r = -0.269		<0.001
(discrete)	Low	1.2%	3.9%	9.2%	<0.001
Intermittent Claudication and Vascular		(n=595)	(n=486)	(n=839)	
Insufficiency Index	Abnormal	2.5%	2.1%	4.1%	0.082

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				
		Never	**Former**	**>0-20**	**>20**	**p-Value**
Essential Hypertension		--	--	--	--	--
	Yes					
Heart Disease (Excluding Essential		--	--	--	--	--
Hypertension)	Yes					

Table F-7. Dependent Variable-covariate Associations for the Cardiovascular Assessment (Continued)

| Dependent Variable | Level | Current Cigarette Smoking (cigarettes/day) | | | | |
		Never	Former	>0-20	>20	p-Value
Myocardial Infarction		--	--	--	--	--
	Yes					
Stroke or Transient Ischemic Attack		--	--	--	--	--
	Yes					
Systolic Blood Pressure (mm Hg)		(n=595)	(n=1,056)	(n=211)	(n=58)	
(continuous)	--		r = -0.075			0.001
(discrete)	High	23.2%	26.9%	20.9%	15.5%	0.051
Diastolic Blood Pressure (mm Hg)		(n=595)	(n=1,056)	(n=211)	(n=58)	
(continuous)	--		r = -0.022			0.339
(discrete)	High	5.7%	4.7%	4.7%	5.2%	0.847
Heart Sounds		(n=595)	(n=1,056)	(n=211)	(n=58)	
	Abnormal	6.1%	5.8%	8.5%	10.3%	0.268
Overall Electrocardiograph (ECG)		(n=595)	(n=1,056)	(n=211)	(n=58)	
	Abnormal	32.6%	38.2%	31.8%	34.5%	0.081
ECG: RBBB		(n=595)	(n=1,056)	(n=211)	(n=58)	
	Yes	3.4%	4.4%	2.8%	3.5%	0.634
ECG: LBBB		(n=595)	(n=1,056)	(n=211)	(n=58)	
	Yes	1.0%	1.3%	0.5%	5.2%	0.035
ECG: Nonspecific ST- and T-wave Changes		(n=595)	(n=1,056)	(n=211)	(n=58)	
	Yes	20.8%	25.3%	21.3%	20.7%	0.171
ECG: Bradycardia		(n=595)	(n=1,056)	(n=211)	(n=58)	
	Yes	5.6%	4.6%	5.2%	5.2%	0.836
ECG: Tachycardia		(n=595)	(n=1,056)	(n=211)	(n=58)	
	Yes	0.3%	0.6%	0.0%	3.5%	0.011
ECG: Arrhythmia		(n=595)	(n=1,056)	(n=211)	(n=58)	
	Yes	9.8%	11.6%	6.6%	6.9%	0.123
ECG: Evidence of Prior Myocardial Infarction		(n=595)	(n=1,056)	(n=211)	(n=58)	
	Yes	3.2%	6.0%	4.7%	3.5%	0.087
Funduscopic Examination		(n=549)	(n=954)	(n=200)	(n=56)	
	Abnormal	7.5%	11.8%	11.5%	16.1%	0.027
Carotid Bruits		(n=595)	(n=1,056)	(n=211)	(n=58)	
	Present	1.2%	2.5%	4.3%	1.7%	0.062
Radial Pulses		(n=590)	(n=1,052)	(n=211)	(n=58)	
	Abnormal	5.8%	7.0%	8.5%	6.9%	0.554
Femoral Pulses		(n=595)	(n=1,057)	(n=211)	(n=58)	
	Abnormal	0.0%	1.0%	4.3%	3.5%	<0.001
Popliteal Pulses		(n=594)	(n=1,056)	(n=210)	(n=58)	
	Abnormal	0.5%	2.6%	6.2%	6.9%	<0.001
Dorsalis Pedis Pulses		(n=594)	(n=1,053)	(n=210)	(n=58)	
	Abnormal	4.0%	9.2%	12.9%	13.8%	<0.001
Posterior Tibial Pulses		(n=594)	(n=1,053)	(n=211)	(n=58)	
	Abnormal	1.5%	5.8%	10.9%	12.1%	<0.001

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				
		Never	Former	>0-20	>20	p-Value
Leg Pulses		(n=593)	(n=1,053)	(n=209)	(n=58)	
	Abnormal	4.6%	10.6%	14.8%	15.5%	<0.001
Peripheral Pulses		(n=588)	(n=1,049)	(n=209)	(n=58)	
	Abnormal	10.0%	16.4%	21.1%	20.7%	<0.001
Resting Pressure Index		(n=589)	(n=1,043)	(n=209)	(n=58)	
(continuous)	--		r = -0.162			<0.001
(discrete)	Low	1.0%	4.6%	6.7%	6.9%	<0.001
Hyperemic Pressure Index (1 minute post-exercise)		(n=577)	(n=1,011)	(n=202)	(n=56)	
(continuous)	--		r = -0.180			<0.001
(discrete)	Low	2.1%	10.8%	17.8%	30.4%	<0.001
Hyperemic Pressure Index (2 minutes post-exercise)		(n=578)	(n=1,012)	(n=202)	(n=56)	
(continuous)	--		r = -0.164			<0.001
(discrete)	Low	1.2%	6.2%	10.9%	12.5%	<0.001
Intermittent Claudication and Vascular Insufficiency Index	Abnormal	(n=595) 2.5%	(n=1,057) 3.6%	(n=211) 2.8%	(n=58) 0.0%	0.327

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	>0-40	>40	p-Value
Essential Hypertension		(n=107)	(n=1,208)	(n=581)	
	Yes	54.2%	52.7%	61.1%	0.003
Heart Disease (Excluding Essential Hypertension)	Yes	(n=107) 81.3%	(n=1,219) 81.3%	(n=588) 84.4%	0.272
Myocardial Infarction		(n=107)	(n=1,219)	(n=588)	
	Yes	14.0%	10.2%	11.7%	0.339
Stroke or Transient Ischemic Attack		(n=107)	(n=1,219)	(n=588)	
	Yes	3.7%	2.7%	4.4%	0.155
Systolic Blood Pressure (mm Hg)		(n=107)	(n=1,218)	(n=588)	
(continuous)	--		r = 0.011		0.634
(discrete)	High	18.7%	24.1%	27.0%	0.135
Diastolic Blood Pressure (mm Hg)		(n=107)	(n=1,218)	(n=588)	
(continuous)	--		r = 0.005		0.825
(discrete)	High	4.7%	5.3%	4.8%	0.888
Heart Sounds		(n=107)	(n=1,218)	(n=588)	
	Abnormal	3.7%	5.3%	9.0%	0.005
Overall Electrocardiograph (ECG)		(n=107)	(n=1,218)	(n=588)	
	Abnormal	34.6%	33.0%	41.2%	0.003
ECG: RBBB		(n=107)	(n=1,218)	(n=588)	
	Yes	1.9%	3.8%	4.4%	0.436
ECG: LBBB		(n=107)	(n=1,218)	(n=588)	
	Yes	1.9%	1.4%	0.9%	0.523

Table F-7. Dependent Variable-covariate Associations for the Cardiovascular Assessment (Continued)

| Dependent Variable | Level | Lifetime Alcohol History (drink-years) | | | |
		0	>0-40	>40	p-Value
ECG: Nonspecific ST- and T-wave Changes	Yes	(n=107) 21.5%	(n=1,218) 23.1%	(n=588) 24.0%	0.826
ECG: Bradycardia	Yes	(n=107) 1.9%	(n=1,218) 4.6%	(n=588) 6.3%	0.095
ECG: Tachycardia	Yes	(n=107) 0.0%	(n=1,218) 0.5%	(n=588) 0.7%	0.649
ECG: Arrhythmia	Yes	(n=107) 12.2%	(n=1,218) 8.8%	(n=588) 13.3%	0.011
ECG: Evidence of Prior Myocardial Infarction	Yes	(n=107) 6.5%	(n=1,218) 4.7%	(n=588) 5.1%	0.672
Funduscopic Examination	Abnormal	(n=95) 13.7%	(n=1,123) 9.5%	(n=536) 12.1%	0.162
Carotid Bruits	Present	(n=107) 0.9%	(n=1,218) 1.9%	(n=588) 3.2%	0.126
Radial Pulses	Abnormal	(n=107) 8.4%	(n=1,213) 6.7%	(n=584) 6.9%	0.793
Femoral Pulses	Abnormal	(n=107) 1.9%	(n=1,219) 0.8%	(n=588) 1.7%	0.200
Popliteal Pulses	Abnormal	(n=106) 2.8%	(n=1,218) 2.0%	(n=587) 3.4%	0.176
Dorsalis Pedis Pulses	Abnormal	(n=106) 8.5%	(n=1,215) 6.8%	(n=587) 11.1%	0.007
Posterior Tibial Pulses	Abnormal	(n=106) 4.7%	(n=1,216) 4.0%	(n=587) 7.8%	0.003
Leg Pulses	Abnormal	(n=105) 9.5%	(n=1,215) 7.8%	(n=586) 12.6%	0.005
Peripheral Pulses	Abnormal	(n=105) 17.1%	(n=1,209) 13.7%	(n=583) 17.8%	0.057
Resting Pressure Index (continuous)	--	(n=106)	(n=1,206) r = -0.106	(n=581)	<0.001
(discrete)	Low	2.8%	3.1%	5.5%	0.036
Hyperemic Pressure Index (1 minute post-exercise) (continuous)	--	(n=101)	(n=1,176) r = -0.108	(n=563)	<0.001
(discrete)	Low	9.9%	7.1%	14.2%	<0.001
Hyperemic Pressure Index (2 minutes post-exercise) (continuous)	--	(n=101)	(n=1,178) r = -0.102	(n=563)	<0.001
(discrete)	Low	4.0%	4.1%	8.4%	<0.001
Intermittent Claudication and Vascular Insufficiency Index	Abnormal	(n=107) 5.6%	(n=1,219) 2.6%	(n=588) 3.4%	0.185

Dependent Variable	Level	Current Alcohol Use (drinks/day)			Uric Acid (mg/dL)		
		0-1	>1	p-Value	≤5.5	>5.5	p-Value
Essential Hypertension		--	--	--	(n=879)	(n=1,026)	
	Yes				50.6%	59.6%	<0.001
Heart Disease (Excluding Essential Hypertension)		--	--	--	(n=888)	(n=1,035)	
	Yes				82.0%	82.4%	0.851
Myocardial Infarction		--	--	--	(n=888)	(n=1,035)	
	Yes				9.8%	11.8%	0.185
Stroke or Transient Ischemic Attack		--	--	--	(n=888)	(n=1,035)	
	Yes				3.3%	3.5%	0.896
Systolic Blood Pressure (mm Hg)		(n=1,631)	(n=289)		(n=887)	(n=1,035)	
(continuous)	--	r = -0.009		0.686	r = 0.064		0.005
(discrete)	High	24.6%	25.6%	0.767	22.3%	26.9%	0.025
Diastolic Blood Pressure (mm Hg)		(n=1,631)	(n=289)		(n=887)	(n=1,035)	
(continuous)	--	r = 0.022		0.331	r = -0.036		0.112
(discrete)	High	4.8%	6.6%	0.256	4.6%	5.4%	0.495
Heart Sounds		(n=1,631)	(n=289)		(n=887)	(n=1,035)	
	Abnormal	6.1%	7.3%	0.548	5.3%	7.3%	0.099
Overall Electrocardiograph (ECG)		(n=1,631)	(n=289)		(n=887)	(n=1,035)	
	Abnormal	35.6%	36.0%	0.942	31.7%	39.0%	<0.001
ECG: RBBB		(n=1,631)	(n=289)		(n=887)	(n=1,035)	
	Yes	4.2%	2.1%	0.124	4.0%	3.8%	0.934
ECG: LBBB		(n=1,631)	(n=289)		(n=887)	(n=1,035)	
	Yes	1.3%	1.0%	0.949	1.0%	1.5%	0.516
ECG: Nonspecific ST- and T-wave Changes		(n=1,631)	(n=289)		(n=887)	(n=1,035)	
	Yes	23.0%	25.3%	0.445	20.3%	26.0%	0.004
ECG: Bradycardia		(n=1,631)	(n=289)		(n=887)	(n=1,035)	
	Yes	4.8%	5.5%	0.724	5.4%	4.5%	0.440
ECG: Tachycardia		(n=1,631)	(n=289)		(n=887)	(n=1,035)	
	Yes	0.4%	1.0%	0.378	0.5%	0.6%	0.942
ECG: Arrhythmia		(n=1,631)	(n=289)		(n=887)	(n=1,035)	
	Yes	9.9%	12.5%	0.232	7.4%	12.8%	<0.001
ECG: Evidence of Prior Myocardial Infarction		(n=1,631)	(n=289)		(n=887)	(n=1,035)	
	Yes	4.9%	4.8%	0.999	4.0%	5.8%	0.078
Funduscopic Examination		(n=1,487)	(n=272)		(n=810)	(n=951)	
	Abnormal	10.8%	9.2%	0.484	8.9%	12.1%	0.036
Carotid Bruits		(n=1,631)	(n=289)		(n=887)	(n=1,035)	
	Present	2.1%	3.1%	0.382	2.9%	1.7%	0.112
Radial Pulses		(n=1,626)	(n=285)		(n=884)	(n=1,029)	
	Abnormal	6.5%	8.4%	0.294	5.5%	7.9%	0.054
Femoral Pulses		(n=1,632)	(n=289)		(n=888)	(n=1,035)	
	Abnormal	1.0%	2.1%	0.189	0.6%	1.6%	0.045
Popliteal Pulses		(n=1,629)	(n=289)		(n=886)	(n=1,034)	
	Abnormal	2.2%	3.8%	0.158	1.5%	3.4%	0.011

Dependent Variable	Level	Current Alcohol Use (drinks/day)			Uric Acid (mg/dL)		
		0-1	>1	p-Value	≤5.5	>5.5	p-Value
Dorsalis Pedis Pulses		(n=1,626)	(n=289)		(n=886)	(n=1,031)	
	Abnormal	7.7%	10.7%	0.104	6.2%	9.9%	0.004
Posterior Tibial Pulses		(n=1,628)	(n=288)		(n=884)	(n=1,034)	
	Abnormal	4.9%	7.3%	0.116	3.9%	6.5%	0.014
Leg Pulses		(n=1,625)	(n=288)		(n=883)	(n=1,032)	
	Abnormal	8.9%	11.8%	0.150	7.1%	11.3%	0.002
Peripheral Pulses		(n=1,619)	(n=285)		(n=879)	(n=1,027)	
	Abnormal	14.5%	18.3%	0.125	12.4%	17.4%	0.003
Resting Pressure Index		(n=1,612)	(n=287)		(n=881)	(n=1,020)	
(continuous)	--	r = -0.038		0.100	r = -0.075		0.001
(discrete)	Low	3.6%	4.9%	0.380	3.1%	4.4%	0.157
Hyperemic Pressure Index							
(1 minute post-exercise)		(n=1,569)	(n=277)		(n=857)	(n=991)	
(continuous)	--	r = -0.039		0.093	r = -0.058		0.013
(discrete)	Low	9.1%	11.6%	0.229	9.1%	9.8%	0.672
Hyperemic Pressure Index							
(2 minutes post-exercise)		(n=1,571)	(n=277)		(n=858)	(n=992)	
(continuous)	--	r = -0.032		0.169	r = -0.061		0.009
(discrete)	Low	5.1%	6.9%	0.289	5.1%	5.5%	0.770
Intermittent Claudication and		(n=1,632)	(n=289)		(n=887)	(n=1,034)	
Vascular Insufficiency Index	Abnormal	3.3%	1.7%	0.212	3.2%	3.0%	0.946

Dependent Variable	Level	Body Mass Index (kg/m^2)			Waist-to-hip Ratio		
		Not Obese (≤30)	Obese (>30)	p-Value	≤1	>1	p-Value
Essential Hypertension		(n=1,236)	(n=669)		(n=976)	(n=928)	
	Yes	48.1%	69.1%	<0.001	48.6%	62.6%	<0.001
Heart Disease (Excluding		(n=1,244)	(n=678)		(n=982)	(n=939)	
Essential Hypertension)	Yes	82.2%	82.3%	0.986	82.4%	82.0%	0.874
Myocardial Infarction		(n=1,244)	(n=678)		(n=982)	(n=939)	
	Yes	10.8%	11.1%	0.906	9.6%	12.3%	0.071
Stroke or Transient Ischemic		(n=1,244)	(n=678)		(n=982)	(n=939)	
Attack	Yes	3.3%	3.5%	0.880	2.6%	4.3%	0.051
Systolic Blood Pressure (mm Hg)		(n=1,244)	(n=678)		(n=982)	(n=939)	
(continuous)	--	r = 0.151		<0.001	r = 0.127		<0.001
(discrete)	High	22.5%	28.9%	0.002	22.3%	27.3%	0.014
Diastolic Blood Pressure (mm Hg)		(n=1,244)	(n=678)		(n=982)	(n=939)	
(continuous)	--	r = 0.070		0.002	r = 0.018		0.423
(discrete)	High	4.7%	5.8%	0.350	5.0%	5.1%	0.986
Heart Sounds		(n=1,244)	(n=678)		(n=982)	(n=939)	
	Abnormal	6.4%	6.3%	0.999	5.5%	7.2%	0.141

Dependent Variable	Level	Body Mass Index (kg/m^2)			Waist-to-hip Ratio		
		Not Obese (≤30)	Obese (>30)	p-Value	≤1	>1	p-Value
Overall Electrocardiograph (ECG)		(n=1,244)	(n=678)		(n=982)	(n=939)	
	Abnormal	34.2%	38.2%	0.093	31.9%	39.5%	<0.001
ECG: RBBB		(n=1,244)	(n=678)		(n=982)	(n=939)	
	Yes	4.2%	3.2%	0.371	3.2%	4.6%	0.133
ECG: LBBB		(n=1,244)	(n=678)		(n=982)	(n=939)	
	Yes	1.2%	1.3%	0.988	1.1%	1.4%	0.752
ECG: Nonspecific ST- and T-wave Changes	Yes	(n=1,244) 21.7%	(n=678) 26.4%	0.023	(n=982) 19.0%	(n=939) 27.8%	<0.001
ECG: Bradycardia		(n=1,244)	(n=678)		(n=982)	(n=939)	
	Yes	5.6%	3.7%	0.078	6.4%	3.4%	0.003
ECG: Tachycardia		(n=1,244)	(n=678)		(n=982)	(n=939)	
	Yes	0.5%	0.6%	0.999	0.4%	0.6%	0.698
ECG: Arrhythmia		(n=1,244)	(n=678)		(n=982)	(n=939)	
	Yes	9.7%	11.5%	0.229	9.1%	11.6%	0.079
ECG: Evidence of Prior Myocardial Infarction	Yes	(n=1,244) 4.3%	(n=678) 6.1%	0.124	(n=982) 4.4%	(n=939) 5.5%	0.287
Funduscopic Examination		(n=1,150)	(n=611)		(n=903)	(n=858)	
	Abnormal	10.0%	11.8%	0.282	7.2%	14.2%	<0.001
Carotid Bruits		(n=1,244)	(n=678)		(n=982)	(n=939)	
	Present	2.4%	2.1%	0.744	1.9%	2.6%	0.444
Radial Pulses		(n=1,237)	(n=675)		(n=978)	(n=933)	
	Abnormal	6.1%	8.0%	0.148	6.2%	7.4%	0.361
Femoral Pulses		(n=1,244)	(n=678)		(n=982)	(n=939)	
	Abnormal	1.1%	1.3%	0.740	1.1%	1.2%	0.999
Popliteal Pulses		(n=1,243)	(n=676)		(n=982)	(n=936)	
	Abnormal	2.7%	2.2%	0.666	1.9%	3.0%	0.178
Dorsalis Pedis Pulses		(n=1,239)	(n=677)		(n=979)	(n=937)	
	Abnormal	8.7%	7.2%	0.298	7.0%	9.5%	0.051
Posterior Tibial Pulses		(n=1,240)	(n=677)		(n=980)	(n=937)	
	Abnormal	6.1%	3.8%	0.050	4.2%	6.4%	0.038
Leg Pulses		(n=1,238)	(n=676)		(n=977)	(n=936)	
	Abnormal	10.2%	8.0%	0.137	7.8%	11.0%	0.019
Peripheral Pulses		(n=1,232)	(n=673)		(n=973)	(n=931)	
	Abnormal	15.5%	14.4%	0.570	13.6%	16.7%	0.070
Resting Pressure Index		(n=1,230)	(n=670)		(n=973)	(n=927)	
(continuous)	--	r = -0.004		0.879	r = -0.123		<0.001
(discrete)	Low	4.2%	3.1%	0.328	3.4%	4.2%	0.418
Hyperemic Pressure Index (1 minute post-exercise)		(n=1,205)	(n=642)		(n=955)	(n=892)	
(continuous)	--	r = -0.065		0.005	r = -0.146		<0.001
(discrete)	Low	9.4%	9.5%	0.997	6.9%	12.1%	<0.001

Dependent Variable	Level	Body Mass Index (kg/m^2)			Waist-to-hip Ratio		
		Not Obese (≤30)	Obese (>30)	p-Value	≤1	>1	p-Value
Hyperemic Pressure Index (2 minutes post-exercise)		(n=1,206)	(n=643)		(n=955)	(n=894)	
(continuous)	--	r = -0.037		0.116	r = -0.136		<0.001
(discrete)	Low	5.8%	4.4%	0.224	4.1%	6.6%	0.021
Intermittent Claudication and Vascular Insufficiency Index	Abnormal	(n=1,242) 2.9%	(n=678) 3.2%	0.776	(n=981) 2.9%	(n=938) 3.2%	0.759

Dependent Variable	Level	Cholesterol (mg/dL)			
		0-200	201-239	≥240	p-Value
Essential Hypertension		(n=1,038)	(n=623)	(n=244)	
	Yes	61.5%	51.4%	40.2%	<0.001
Heart Disease (Excluding Essential Hypertension)		(n=1,048)	(n=631)	(n=244)	
	Yes	83.9%	81.9%	75.8%	0.012
Myocardial Infarction		(n=1,048)	(n=631)	(n=244)	
	Yes	15.3%	6.2%	4.1%	<0.001
Stroke or Transient Ischemic Attack		(n=1,048)	(n=631)	(n=244)	
	Yes	4.1%	2.7%	2.1%	0.142
Systolic Blood Pressure (mm Hg)		(n=1,047)	(n=631)	(n=244)	
(continuous)	--		r = 0.068		0.003
(discrete)	High	24.0%	24.7%	28.3%	0.374
Diastolic Blood Pressure (mm Hg)		(n=1,047)	(n=631)	(n=244)	
(continuous)	--		r = 0.161		<0.001
(discrete)	High	3.6%	5.2%	10.7%	<0.001
Heart Sounds		(n=1,047)	(n=631)	(n=244)	
	Abnormal	7.3%	6.0%	3.3%	0.066
Overall Electrocardiograph (ECG)		(n=1,047)	(n=631)	(n=244)	
	Abnormal	38.9%	33.4%	27.5%	0.001
ECG: RBBB		(n=1,047)	(n=631)	(n=244)	
	Yes	4.8%	3.2%	1.6%	0.040
ECG: LBBB		(n=1,047)	(n=631)	(n=244)	
	Yes	1.2%	1.6%	0.8%	0.597
ECG: Nonspecific ST- and T-wave Changes		(n=1,047)	(n=631)	(n=244)	
	Yes	25.1%	22.5%	18.0%	0.051
ECG: Bradycardia		(n=1,047)	(n=631)	(n=244)	
	Yes	5.2%	5.1%	3.7%	0.624
ECG: Tachycardia		(n=1,047)	(n=631)	(n=244)	
	Yes	0.5%	0.8%	0.0%	0.330
ECG: Arrhythmia		(n=1,047)	(n=631)	(n=244)	
	Yes	11.4%	9.8%	7.0%	0.112
ECG: Evidence of Prior Myocardial Infarction		(n=1,047)	(n=631)	(n=244)	
	Yes	6.6%	3.5%	1.6%	<0.001

Dependent Variable	Level	Cholesterol (mg/dL)			
		0-200	201-239	≥240	p-Value
Funduscopic Examination		(n=954)	(n=579)	(n=228)	
	Abnormal	12.5%	7.9%	9.7%	0.018
Carotid Bruits		(n=1,047)	(n=631)	(n=244)	
	Present	2.9%	2.2%	0.0%	0.026
Radial Pulses		(n=1,043)	(n=627)	(n=243)	
	Abnormal	6.3%	7.0%	8.2%	0.549
Femoral Pulses		(n=1,048)	(n=631)	(n=244)	
	Abnormal	1.4%	0.8%	0.8%	0.431
Popliteal Pulses		(n=1,047)	(n=629)	(n=244)	
	Abnormal	3.0%	2.2%	1.2%	0.256
Dorsalis Pedis Pulses		(n=1,043)	(n=630)	(n=244)	
	Abnormal	10.3%	5.7%	5.7%	0.002
Posterior Tibial Pulses		(n=1,044)	(n=630)	(n=244)	
	Abnormal	6.0%	4.4%	4.1%	0.252
Leg Pulses		(n=1,042)	(n=629)	(n=244)	
	Abnormal	11.5%	6.5%	7.8%	0.002
Peripheral Pulses		(n=1,038)	(n=625)	(n=243)	
	Abnormal	16.3%	13.0%	15.6%	0.181
Resting Pressure Index		(n=1,030)	(n=629)	(n=242)	
(continuous)	--		r = 0.002		0.934
(discrete)	Low	4.1%	2.9%	5.0%	0.269
Hyperemic Pressure Index (1 minute post-exercise)		(n=997)	(n=614)	(n=237)	
(continuous)	--		r = -0.001		0.980
(discrete)	Low	10.6%	8.0%	8.4%	0.178
Hyperemic Pressure Index (2 minutes post-exercise)		(n=997)	(n=616)	(n=237)	
(continuous)	--		r = -0.003		0.890
(discrete)	Low	5.9%	4.2%	5.9%	0.312
Intermittent Claudication and Vascular Insufficiency Index		(n=1,047)	(n=630)	(n=244)	
	Abnormal	4.0%	1.9%	2.1%	0.033

Dependent Variable	Level	HDL (mg/dL)			Cholesterol-HDL Ratio		
		0-35	>35	p-Value	0-5	>5	p-Value
Essential Hypertension		(n=366)	(n=1,539)		(n=1,296)	(n=609)	
	Yes	62.0%	53.9%	0.006	57.3%	51.6%	0.023
Heart Disease (Excluding Essential Hypertension)		(n=370)	(n=1,553)		(n=1,309)	(n=614)	
	Yes	82.4%	82.2%	0.963	84.0%	78.3%	0.003
Myocardial Infarction		(n=370)	(n=1,553)		(n=1,309)	(n=614)	
	Yes	13.0%	10.4%	0.176	12.2%	8.0%	0.007
Stroke or Transient Ischemic Attack		(n=370)	(n=1,553)		(n=1,309)	(n=614)	
	Yes	2.2%	3.7%	0.200	3.9%	2.3%	0.091

Dependent Variable	Level	HDL (mg/dL)			Cholesterol-HDL Ratio		
		0-35	>35	p-Value	0-5	>5	p-Value
Systolic Blood Pressure (mm Hg)		(n=370)	(n=1,552)		(n=1,308)	(n=614)	
(continuous)	--	r = -0.027		0.241	r = 0.079		<0.001
(discrete)	High	28.4%	23.9%	0.085	24.4%	25.6%	0.615
Diastolic Blood Pressure (mm Hg)		(n=370)	(n=1,552)		(n=1,308)	(n=614)	
(continuous)	--	r = 0.004		0.870	r = 0.093		<0.001
(discrete)	High	3.8%	5.4%	0.270	5.1%	5.1%	0.999
Heart Sounds		(n=370)	(n=1,552)		(n=1,308)	(n=614)	
	Abnormal	8.1%	5.9%	0.154	7.0%	4.9%	0.089
Overall Electrocardiograph (ECG)		(n=370)	(n=1,552)		(n=1,308)	(n=614)	
	Abnormal	38.7%	34.9%	0.199	37.7%	31.3%	0.007
ECG: RBBB		(n=370)	(n=1,552)		(n=1,308)	(n=614)	
	Yes	4.3%	3.7%	0.706	4.4%	2.6%	0.070
ECG: LBBB		(n=370)	(n=1,552)		(n=1,308)	(n=614)	
	Yes	3.0%	0.8%	0.002	1.1%	1.6%	0.419
ECG: Nonspecific ST- and T-wave Changes		(n=370)	(n=1,552)		(n=1,308)	(n=614)	
	Yes	27.3%	22.4%	0.055	24.7%	20.5%	0.050
ECG: Bradycardia		(n=370)	(n=1,552)		(n=1,308)	(n=614)	
	Yes	3.2%	5.4%	0.122	5.9%	2.9%	0.008
ECG: Tachycardia		(n=370)	(n=1,552)		(n=1,308)	(n=614)	
	Yes	0.5%	0.5%	0.999	0.6%	0.3%	0.637
ECG: Arrhythmia		(n=370)	(n=1,552)		(n=1,308)	(n=614)	
	Yes	10.0%	10.4%	0.907	10.5%	9.9%	0.778
ECG: Evidence of Prior Myocardial Infarction		(n=370)	(n=1,552)		(n=1,308)	(n=614)	
	Yes	7.0%	4.5%	0.054	5.4%	4.1%	0.274
Funduscopic Examination		(n=327)	(n=1,434)		(n=1,198)	(n=563)	
	Abnormal	12.8%	10.1%	0.178	11.4%	9.1%	0.169
Carotid Bruits		(n=370)	(n=1,552)		(n=1,308)	(n=614)	
	Present	2.7%	2.2%	0.690	2.8%	1.3%	0.069
Radial Pulses		(n=368)	(n=1,545)		(n=1,300)	(n=613)	
	Abnormal	6.8%	6.8%	0.999	6.5%	7.3%	0.580
Femoral Pulses		(n=370)	(n=1,553)		(n=1,309)	(n=614)	
	Abnormal	1.4%	1.1%	0.885	1.0%	1.5%	0.497
Popliteal Pulses		(n=370)	(n=1,550)		(n=1,307)	(n=613)	
	Abnormal	2.4%	2.5%	0.999	2.7%	2.1%	0.567
Dorsalis Pedis Pulses		(n=368)	(n=1,549)		(n=1,305)	(n=612)	
	Abnormal	9.0%	8.0%	0.618	8.8%	6.9%	0.173
Posterior Tibial Pulses		(n=370)	(n=1,548)		(n=1,305)	(n=613)	
	Abnormal	6.0%	5.1%	0.601	5.5%	4.7%	0.542
Leg Pulses		(n=368)	(n=1,547)		(n=1,304)	(n=611)	
	Abnormal	10.9%	9.1%	0.329	9.7%	8.8%	0.623
Peripheral Pulses		(n=366)	(n=1,540)		(n=1,296)	(n=610)	
	Abnormal	16.1%	14.9%	0.604	15.1%	15.1%	0.999

Table F-7. Dependent Variable-covariate Associations for the Cardiovascular Assessment (Continued)

Dependent Variable	Level	HDL (mg/dL)			Cholesterol-HDL Ratio		
		0-35	>35	p-Value	0-5	>5	p-Value
Resting Pressure Index		(n=366)	(n=1,535)		(n=1,294)	(n=607)	
(continuous)	--	r = 0.024		0.290	r = -0.029		0.214
(discrete)	Low	2.2%	4.2%	0.102	4.3%	2.8%	0.157
Hyperemic Pressure Index							
(1 minute post-exercise)		(n=348)	(n=1,500)		(n=1,263)	(n=585)	
(continuous)	--	r = 0.062		0.007	r = -0.055		0.018
(discrete)	Low	10.3%	9.3%	0.605	9.8%	8.7%	0.506
Hyperemic Pressure Index							
(2 minutes post-exercise)		(n=348)	(n=1,502)		(n=1,265)	(n=585)	
(continuous)	--	r = 0.042		0.070	r =-0.039		0.095
(discrete)	Low	4.6%	5.5%	0.575	6.0%	3.9%	0.083
Intermittent Claudication and		(n=369)	(n=1,552)		(n=1,308)	(n=613)	
Vascular Insufficiency Index	Abnormal	3.8%	2.9%	0.467	3.2%	2.8%	0.707

Dependent Variable	Level	Family History of Heart Disease			Family History of Heart Disease Before Age 45		
		No	Yes	p-Value	No	Yes	p-Value
Essential Hypertension		(n=691)	(n=1,203)		(n=1,671)	(n=186)	
	Yes	48.2%	59.5%	<0.001	54.2%	61.8%	0.057
Heart Disease (Excluding		(n=693)	(n=1,219)		(n=1,683)	(n=190)	
Essential Hypertension)	Yes	79.5%	83.8%	0.023	81.8%	84.7%	0.361
Myocardial Infarction		(n=693)	(n=1,219)		(n=1,683)	(n=190)	
	Yes	6.4%	13.4%	<0.001	10.3%	15.8%	0.028
Stroke or Transient Ischemic		(n=693)	(n=1,219)		(n=1,683)	(n=190)	
Attack	Yes	3.2%	3.5%	0.854	3.3%	4.2%	0.638
Systolic Blood Pressure (mm Hg)		(n=693)	(n=1,218)		(n=1,682)	(n=190)	
(continuous)	--	ō = 128.6	ō = 128.8	0.829	ō = 128.8	ō = 127.6	0.362
(discrete)	High	24.1%	25.2%	0.629	25.3%	21.6%	0.297
Diastolic Blood Pressure (mm Hg)		(n=693)	(n=1,218)		(n=1,682)	(n=190)	
(continuous)	--	ō = 75.58	ō = 74.55	0.024	ō = 75.00	ō = 74.45	0.459
(discrete)	High	6.8%	4.1%	0.014	5.2%	4.7%	0.933
Heart Sounds		(n=693)	(n=1,218)		(n=1,682)	(n=190)	
	Abnormal	6.2%	6.4%	0.941	6.4%	5.3%	0.642
Overall Electrocardiograph (ECG)		(n=693)	(n=1,218)		(n=1,682)	(n=190)	
	Abnormal	30.5%	38.6%	<0.001	34.8%	41.6%	0.076
ECG: RBBB		(n=693)	(n=1,218)		(n=1,682)	(n=190)	
	Yes	2.9%	4.4%	0.118	3.7%	3.7%	0.999
ECG: LBBB		(n=693)	(n=1,218)		(n=1,682)	(n=190)	
	Yes	1.4%	1.2%	0.734	1.3%	1.1%	0.999
ECG: Nonspecific ST- and		(n=693)	(n=1,218)		(n=1,682)	(n=190)	
T-wave Changes	Yes	19.9%	25.4%	0.008	22.4%	31.1%	0.010

Dependent Variable	Level	Family History of Heart Disease			Family History of Heart Disease Before Age 45		
		No	Yes	p-Value	No	Yes	p-Value
ECG: Bradycardia		(n=693)	(n=1,218)		(n=1,682)	(n=190)	
	Yes	4.5%	5.1%	0.623	4.8%	5.3%	0.925
ECG: Tachycardia		(n=693)	(n=1,218)		(n=1,682)	(n=190)	
	Yes	0.3%	0.7%	0.458	0.5%	0.5%	0.999
ECG: Arrhythmia		(n=693)	(n=1,218)		(n=1,682)	(n=190)	
	Yes	9.5%	10.8%	0.408	10.3%	12.1%	0.515
ECG: Evidence of Prior Myocardial Infarction	Yes	(n=693) 2.9%	(n=1,218) 6.1%	0.003	(n=1,682) 4.6%	(n=190) 7.9%	0.075
Funduscopic Examination		(n=645)	(n=1,106)		(n=1,547)	(n=170)	
	Abnormal	10.4%	10.5%	0.999	10.2%	11.2%	0.796
Carotid Bruits		(n=693)	(n=1,218)		(n=1,682)	(n=190)	
	Present	1.6%	2.6%	0.189	2.1%	3.7%	0.248
Radial Pulses		(n=691)	(n=1,211)		(n=1,674)	(n=189)	
	Abnormal	6.4%	7.1%	0.606	7.1%	4.8%	0.290
Femoral Pulses		(n=693)	(n=1,219)		(n=1,683)	(n=190)	
	Abnormal	0.7%	1.4%	0.270	0.8%	2.6%	0.049
Popliteal Pulses		(n=692)	(n=1,217)		(n=1,680)	(n=190)	
	Abnormal	1.6%	3.0%	0.089	2.0%	5.8%	0.002
Dorsalis Pedis Pulses		(n=691)	(n=1,215)		(n=1,678)	(n=189)	
	Abnormal	6.5%	9.1%	0.055	7.8%	10.6%	0.223
Posterior Tibial Pulses		(n=692)	(n=1,215)		(n=1,678)	(n=190)	
	Abnormal	4.3%	5.8%	0.216	4.6%	10.0%	0.003
Leg Pulses		(n=690)	(n=1,214)		(n=1,676)	(n=189)	
	Abnormal	7.7%	10.4%	0.063	8.8%	13.2%	0.065
Peripheral Pulses		(n=688)	(n=1,207)		(n=1,668)	(n=188)	
	Abnormal	13.2%	16.2%	0.091	14.9%	16.5%	0.630
Resting Pressure Index		(n=683)	(n=1,207)		(n=1,668)	(n=183)	
(continuous)	--	O = 1.254	O = 1.252	0.723	O = 1.255	O = 1.240	0.186
(discrete)	Low	2.8%	4.4%	0.103	3.3%	7.1%	0.017
Hyperemic Pressure Index (1 minute post-exercise)		(n=663)	(n=1,174)		(n=1,622)	(n=179)	
(continuous)	--	O = 1.181	O = 1.170	0.236	O = 1.176	O = 1.166	0.493
(discrete)	Low	8.3%	9.9%	0.299	9.1%	10.6%	0.606
Hyperemic Pressure Index (2 minutes post-exercise)		(n=663)	(n=1,176)		(n=1,623)	(n=180)	
(continuous)	--	O = 1.232	O = 1.226	0.446	O = 1.231	O = 1.218	0.348
(discrete)	Low	4.5%	5.9%	0.264	5.1%	7.8%	0.171
Intermittent Claudication and Vascular Insufficiency Index	Abnormal	(n=693) 2.5%	(n=1,219) 3.5%	0.285	(n=1,683) 3.0%	(n=190) 4.2%	0.475

Dependent Variable	Level	Diabetic Class			p-Value
		Normal	Impaired	Diabetic	
Essential Hypertension		(n=1,151)	(n=397)	(n=357)	
	Yes	46.1%	58.9%	81.8%	<0.001
Heart Disease (Excluding Essential Hypertension)	Yes	(n=1,160) 80.1%	(n=400) 83.3%	(n=363) 87.9%	0.003
Myocardial Infarction		(n=1,160)	(n=400)	(n=363)	
	Yes	8.7%	11.0%	17.6%	<0.001
Stroke or Transient Ischemic Attack		(n=1,160)	(n=400)	(n=363)	
	Yes	2.8%	3.5%	5.2%	0.074
Systolic Blood Pressure (mm Hg)		(n=1,159)	(n=400)	(n=363)	
(continuous)	--	O = 127.3	O = 130.2	O = 131.4	<0.001
(discrete)	High	21.7%	28.5%	30.6%	<0.001
Diastolic Blood Pressure (mm Hg)		(n=1,159)	(n=400)	(n=363)	
(continuous)	--	O = 75.69	O = 74.81	O = 72.49	<0.001
(discrete)	High	5.1%	6.5%	3.3%	0.131
Heart Sounds		(n=1,159)	(n=400)	(n=363)	
	Abnormal	5.1%	5.5%	11.3%	<0.001
Overall Electrocardiograph (ECG)		(n=1,159)	(n=400)	(n=363)	
	Abnormal	30.0%	39.3%	49.6%	<0.001
ECG: RBBB		(n=1,159)	(n=400)	(n=363)	
	Yes	3.1%	3.5%	6.6%	0.009
ECG: LBBB		(n=1,159)	(n=400)	(n=363)	
	Yes	1.0%	1.3%	2.2%	0.171
ECG: Nonspecific ST- and T-wave Changes	Yes	(n=1,159) 18.8%	(n=400) 25.0%	(n=363) 36.1%	<0.001
ECG: Bradycardia		(n=1,159)	(n=400)	(n=363)	
	Yes	6.3%	3.5%	2.2%	0.002
ECG: Tachycardia		(n=1,159)	(n=400)	(n=363)	
	Yes	0.4%	1.3%	0.3%	0.073
ECG: Arrhythmia		(n=1,159)	(n=400)	(n=363)	
	Yes	8.1%	13.0%	14.3%	<0.001
ECG: Evidence of Prior Myocardial Infarction	Yes	(n=1,159) 3.6%	(n=400) 5.3%	(n=363) 8.8%	<0.001
Funduscopic Examination		(n=1,078)	(n=369)	(n=314)	
	Abnormal	6.5%	10.8%	24.5%	<0.001
Carotid Bruits		(n=1,159)	(n=400)	(n=363)	
	Present	1.5%	3.0%	4.1%	0.007
Radial Pulses		(n=1,154)	(n=396)	(n=363)	
	Abnormal	6.9%	6.8%	6.3%	0.925
Femoral Pulses		(n=1,160)	(n=400)	(n=363)	
	Abnormal	0.8%	1.3%	2.2%	0.081

Dependent Variable	Level	Diabetic Class			
		Normal	Impaired	Diabetic	p-Value
Popliteal Pulses		(n=1,159)	(n=400)	(n=361)	
	Abnormal	1.6%	2.0%	6.1%	<0.001
Dorsalis Pedis Pulses		(n=1,158)	(n=398)	(n=361)	
	Abnormal	5.9%	6.5%	17.5%	<0.001
Posterior Tibial Pulses		(n=1,158)	(n=399)	(n=361)	
	Abnormal	3.4%	5.3%	11.4%	<0.001
Leg Pulses		(n=1,158)	(n=397)	(n=360)	
	Abnormal	6.8%	7.8%	19.4%	<0.001
Peripheral Pulses		(n=1,152)	(n=394)	(n=360)	
	Abnormal	13.1%	13.5%	23.3%	<0.001
Resting Pressure Index		(n=1,152)	(n=398)	(n=351)	
(continuous)	--	Ō = 1.272	Ō = 1.232	Ō = 1.211	<0.001
(discrete)	Low	2.2%	4.5%	8.3%	<0.001
Hyperemic Pressure Index (1 minute post-exercise)		(n=1,134)	(n=386)	(n=328)	
(continuous)	--	Ō = 1.199	Ō = 1.157	Ō = 1.103	<0.001
(discrete)	Low	6.0%	10.6%	20.1%	<0.001
Hyperemic Pressure Index (2 minutes post-exercise)		(n=1,135)	(n=386)	(n=329)	
(continuous)	--	Ō = 1.250	Ō = 1.216	Ō = 1.166	<0.001
(discrete)	Low	3.2%	5.7%	12.5%	<0.001
Intermittent Claudication and Vascular Insufficiency Index	Abnormal	(n=1,159) 1.7%	(n=400) 3.8%	(n=362) 6.6%	<0.001

Dependent Variable	Level	Currently Taking Blood Pressure Medication			Length of Exercise Prior to Peripheral Blood Pressure Measurements (seconds)		
		No	Yes	p-Value	<120	120	p-Value
Systolic Blood Pressure (mm Hg)		(n=1,074)	(n=848)		--	--	--
(continuous)	--	Ō = 128.6	Ō = 128.8	0.858			
(discrete)	High	23.7%	26.2%	0.222			
Diastolic Blood Pressure (mm Hg)		(n=1,074)	(n=848)		--	--	--
(continuous)	--	Ō = 76.13	Ō = 73.36	<0.001			
(discrete)	High	5.6%	4.4%	0.266			
Hyperemic Pressure Index (1 minute post-exercise)		--	--	--	(n=82)	(n=1,766)	
(continuous)	--				r = 0.183		<0.001
(discrete)	Low				34.2%	8.3%	<0.001

Dependent Variable	Level	Currently Taking Blood Pressure Medication			Length of Exercise Prior to Peripheral Blood Pressure Measurements (seconds)		
		No	Yes	p-Value	<120	120	p-Value
Hyperemic Pressure Index (2 minutes post-exercise)		--	--	--	(n=82)	(n=1,768)	
(continuous)	--				r=0.191		<0.001
(discrete)	Low				22.0%	4.6%	<0.001

--: Covariate is not applicable for this dependent variable.

Note: Correlations (r) are based on total sample size and are not category-specific.

Please see Section 15.1.3 and Table 15-1 for a further discussion of the dependent variables and covariates shown in this appendix.

Table F-8. Dependent Variable-covariate Associations for the Hematology Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
RBC Count (million/mm^3)		(n=882)	(n=1,060)		(n=124)	(n=1,818)	
(continuous)	--	r = -0.231		<0.001	O = 5.04	O = 4.98	0.154
(discrete)	Abnormal Low	4.0%	10.0%	<0.001	6.5%	7.3%	0.001
	Normal	93.3%	87.9%		86.3%	90.7%	
	Abnormal High	2.7%	2.1%		7.3%	2.0%	
WBC Count (thousand/mm^3)		(n=882)	(n=1,060)		(n=124)	(n=1,818)	
(continuous)[a]	--	r = -0.027		0.229	O = 5.69	O = 6.20	0.001
(discrete)	Abnormal Low	10.1%	10.7%	0.863	21.8%	9.6%	<0.001
	Normal	87.9%	87.1%		76.6%	88.2%	
	Abnormal High	2.0%	2.3%		1.6%	2.2%	
Hemoglobin (gm/dL)		(n=882)	(n=1,060)		(n=124)	(n=1,818)	
(continuous)	--	r = -0.198		<0.001	O = 14.75	O = 15.31	<0.001
(discrete)	Abnormal Low	7.8%	14.5%	<0.001	27.4%	10.4%	<0.001
	Normal	91.3%	84.9%		72.6%	88.8%	
	Abnormal High	0.9%	0.6%		0.0%	0.8%	
Hematocrit (percent)		(n=882)	(n=1,060)		(n=124)	(n=1,818)	
(continuous)	--	r = -0.162		<0.001	O = 44.90	O = 45.81	0.012
(discrete)	Abnormal Low	3.2%	6.2%	0.008	9.7%	4.5%	0.021
	Normal	96.0%	92.9%		90.3%	94.6%	
	Abnormal High	0.8%	0.9%		0.0%	0.9%	
Platelet Count (thousand/mm^3)		(n=880)	(n=1,058)		(n=124)	(n=1,814)	
(continuous)[b]	--	r = -0.145		<0.001	O = 245.8	O = 235.0	0.049
(discrete)	Abnormal Low	1.7%	1.8%	0.809	0.8%	1.8%	0.692
	Normal	97.2%	97.4%		98.4%	97.2%	
	Abnormal High	1.1%	0.9%		0.8%	1.0%	
RBC Morphology		(n=882)	(n=1,060)		(n=124)	(n=1,818)	
	Abnormal	4.0%	7.3%	0.003	17.7%	5.0%	<0.001
Absolute Neutrophils (segs) (thousand/mm^3)[b]		(n=1,942)			(n=124)	(n=1,818)	
	--	r = 0.004		0.850	O = 3.19	O = 3.67	<0.001
Absolute Neutrophils (bands) (thousand/mm^3)		(n=1,558)			(n=89)	(n=1,469)	
(continuous)[a]	Nonzero	r = 0.048		0.061	O = 0.129	O = 0.173	0.001
(discrete)		(n=882)	(n=1,060)		(n=124)	(n=1,818)	
	Zero	20.5%	19.2%	0.485	28.2%	19.2%	0.020
Absolute Lymphocytes (thousand/mm^3)[a]		(n=1,942)			(n=124)	(n=1,818)	
	--	r = -0.122		<0.001	O = 1.73	O = 1.63	0.134
Absolute Monocytes (thousand/mm^3)[b]		(n=1,942)			(n=124)	(n=1,818)	
	--	r = 0.019		0.406	O = 0.416	O = 0.419	0.891

Table F-8. Dependent Variable-covariate Associations for the Hematology Assessment (Continued)

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Absolute Eosinophils (thousand/mm³)		(n=1,744)			(n=108)	(n=1,636)	
(continuous)[a]	Nonzero	r = 0.010		0.687	O = 0.148	O = 0.158	0.373
(discrete)		(n=882)	(n=1,060)		(n=124)	(n=1,818)	
	Zero	9.9%	10.5%	0.715	12.9%	10.0%	0.381
Absolute Basophils (thousand/mm³)		(n=1,017)			(n=60)	(n=957)	
(continuous)[a]	Nonzero	r = -0.027		0.389	O = 0.071	O = 0.077	0.215
(discrete)		(n=882)	(n=1,060)		(n=124)	(n=1,818)	
	Zero	49.2%	46.3%	0.222	51.6%	47.4%	0.410
Fibrinogen (mg/dL)		(n=882)	(n=1,059)		(n=124)	(n=1,817)	
(continuous)[a]	--	r = 0.160		<0.001	O = 372.0	O = 354.0	0.003
(discrete)	High	4.4%	6.8%	0.032	10.5%	5.4%	0.031
Erythrocyte Sedimentation Rate (mm/hr)		(n=882)	(n=1,060)		(n=124)	(n=1,818)	
(continuous)[c]	--	r = 0.159		<0.001	O = 8.83	O = 7.36	0.041
(discrete)	Abnormal	7.6%	13.2%	<0.001	16.1%	10.3%	0.059

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
RBC Count (million/mm³)		(n=766)	(n=318)	(n=858)	
(continuous)	--	O = 4.89	O = 5.00	O = 5.05	<0.001
(discrete)	Abnormal Low	9.9%	6.9%	5.0%	<0.001
	Normal	88.8%	89.6%	92.1%	
	Abnormal High	1.3%	3.5%	2.9%	
WBC Count (thousand/mm³)		(n=766)	(n=318)	(n=858)	
(continuous)[a]	--	O = 5.89	O = 6.23	O = 6.40	<0.001
(discrete)	Abnormal Low	11.5%	12.9%	8.5%	0.018
	Normal	87.2%	83.7%	89.0%	
	Abnormal High	1.3%	3.5%	2.5%	
Hemoglobin (gm/dL)		(n=766)	(n=318)	(n=858)	
(continuous)	--	O = 15.13	O = 15.34	O = 15.39	<0.001
(discrete)	Abnormal Low	13.5%	11.3%	9.8%	0.065
	Normal	86.3%	87.7%	89.2%	
	Abnormal High	0.3%	0.9%	1.1%	
Hematocrit (percent)		(n=766)	(n=318)	(n=858)	
(continuous)	--	O = 45.20	O = 46.03	O = 46.14	<0.001
(discrete)	Abnormal Low	6.1%	4.1%	4.0%	0.112
	Normal	93.5%	94.7%	1.1%	
	Abnormal High	0.4%	1.3%	95.0%	

Table F-8. Dependent Variable-covariate Associations for the Hematology Assessment (Continued)

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Platelet Count (thousand/mm^3)		(n=765)	(n=317)	(n=856)	
(continuous)[b]	--	O = 228.2	O = 233.7	O = 243.2	<0.001
(discrete)	Abnormal Low	2.0%	1.9%	1.5%	0.118
	Normal	97.7%	97.5%	96.9%	
	Abnormal High	0.4%	0.6%	1.6%	
RBC Morphology		(n=766)	(n=318)	(n=858)	
	Abnormal	6.4%	6.3%	5.0%	0.445
Absolute Neutrophils (segs) (thousand/mm^3)[b]		(n=766)	(n=318)	(n=858)	
	--	O = 3.47	O = 3.73	O = 3.76	<0.001
Absolute Neutrophils (bands) (thousand/mm^3)		(n=622)	(n=253)	(n=683)	
(continuous)[a]	Nonzero	O = 0.167	O = 0.173	O = 0.173	0.689
(discrete)		(n=766)	(n=318)	(n=858)	
	Zero	18.8%	20.4%	20.4%	0.685
Absolute Lymphocytes (thousand/mm^3)[a]		(n=766)	(n=318)	(n=858)	
	--	O = 1.54	O = 1.63	O = 1.74	<0.001
Absolute Monocytes (thousand/mm^3)[b]		(n=766)	(n=318)	(n=858)	
	--	O = 0.405	O = 0.414	O = 0.432	0.042
Absolute Eosinophils (thousand/mm^3)		(n=691)	(n=289)	(n=764)	
(continuous)[a]	Nonzero	O = 0.149	O = 0.169	O = 0.161	0.021
(discrete)		(n=766)	(n=318)	(n=858)	
	Zero	9.8%	9.1%	11.0%	0.583
Absolute Basophils (thousand/mm^3)		(n=401)	(n=176)	(n=440)	
(continuous)[a]	Nonzero	O = 0.074	O = 0.077	O = 0.078	0.097
(discrete)		(n=766)	(n=318)	(n=858)	
	Zero	47.7%	44.7%	48.7%	0.464
Fibrinogen (mg/dL)		(n=765)	(n=318)	(n=858)	
(continuous)[a]	--	O = 347.4	O = 364.8	O = 358.5	<0.001
(discrete)	High	4.2%	8.8%	5.9%	0.011
Erythrocyte Sedimentation Rate (mm/hr)		(n=766)	(n=318)	(n=858)	
(continuous)[c]	--	O = 6.92	O = 8.34	O = 7.62	0.009
(discrete)	Abnormal	8.8%	12.9%	11.5%	0.071

Table F-8. Dependent Variable-covariate Associations for the Hematology Assessment (Continued)

Dependent Variable	Level	Never	Former	>0–20	>20	p-Value
			Current Cigarette Smoking (cigarettes/day)			
RBC Count (million/mm^3)		(n=598)	(n=1,076)	(n=209)	(n=57)	
(continuous)	--		r = 0.073			0.001
(discrete)	Abnormal Low	6.5%	8.3%	5.3%	3.5%	0.005
	Normal	90.6%	90.2%	89.0%	94.7%	
	Abnormal High	2.8%	1.5%	5.7%	1.8%	
WBC Count (thousand/mm^3)		(n=598)	(n=1,076)	(n=209)	(n=57)	
(continuous)[a]	--		r = 0.292			<0.001
(discrete)	Abnormal Low	14.7%	10.2%	1.4%	1.8%	<0.001
	Normal	84.3%	87.7%	93.8%	91.2%	
	Abnormal High	1.0%	2.0%	4.8%	7.0%	
Hemoglobin (gm/dL)		(n=598)	(n=1,076)	(n=209)	(n=57)	
(continuous)	--		r = 0.167			<0.001
(discrete)	Abnormal Low	12.0%	13.1%	4.3%	1.8%	<0.001
	Normal	87.0%	86.6%	93.3%	98.3%	
	Abnormal High	1.0%	0.3%	2.4%	0.0%	
Hematocrit (percent)		(n=598)	(n=1,076)	(n=209)	(n=57)	
(continuous)	--		r = 0.176			<0.001
(discrete)	Abnormal Low	5.2%	5.5%	1.9%	0.0%	0.002
	Normal	94.0%	94.1%	95.2%	100.0%	
	Abnormal High	0.8%	0.5%	2.9%	0.0%	
Platelet Count (thousand/mm^3)		(n=596)	(n=1,074)	(n=209)	(n=57)	
(continuous)[b]	--		r = 0.073			0.001
(discrete)	Abnormal Low	1.7%	1.9%	1.9%	0.0%	0.375
	Normal	97.8%	97.0%	97.1%	96.5%	
	Abnormal High	0.5%	1.1%	1.0%	3.5%	
RBC Morphology		(n=598)	(n=1,076)	(n=209)	(n=57)	
	Abnormal	5.7%	6.3%	4.8%	0.0%	0.215
Absolute Neutrophils (segs) (thousand/mm^3)[b]	--		(n=1,940) r = 0.271			<0.001
Absolute Neutrophils (bands) (thousand/mm^3) (continuous)[a]	Nonzero		(n=1,557) r = 0.137			<0.001
(discrete)		(n=598)	(n=1,076)	(n=209)	(n=57)	
	Zero	22.2%	18.6%	19.6%	15.8%	0.281
Absolute Lymphocytes (thousand/mm^3)[a]	--		(n=1,940) r = 0.150			<0.001
Absolute Monocytes (thousand/mm^3)[b]	--		(n=1,940) r = 0.158			<0.001
Absolute Eosinophils (thousand/mm^3) (continuous)[a]	Nonzero		(n=1,742) r = 0.121			<0.001
(discrete)		(n=598)	(n=1,076)	(n=209)	(n=57)	
	Zero	11.2%	10.3%	7.2%	8.8%	0.410

Table F-8. Dependent Variable-covariate Associations for the Hematology Assessment (Continued)

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				
		Never	Former	>0–20	>20	p-Value
Absolute Basophils (thousand/mm^3) (continuous)[a]	Nonzero		(n=1,015) r = 0.111			<0.001
(discrete)		(n=598)	(n=1,076)	(n=209)	(n=57)	
	Zero	49.3%	46.8%	48.8%	42.1%	0.621
Fibrinogen (mg/dL)		(n=597)	(n=1,076)	(n=209)	(n=57)	
(continuous)[a]	--		r = 0.130			<0.001
(discrete)	High	3.9%	6.0%	9.1%	8.8%	0.025
Erythrocyte Sedimentation Rate (mm/hr)		(n=598)	(n=1,076)	(n=209)	(n=57)	
(continuous)[c]	--		r = -0.038			0.098
(discrete)	Abnormal	9.2%	11.8%	10.1%	7.0%	0.297

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	>0–10	>10	p-Value
RBC Count (million/mm^3)		(n=598)	(n=488)	(n=853)	
(continuous)	--		r = -0.081		<0.001
(discrete)	Abnormal Low	6.5%	5.1%	9.0%	0.047
	Normal	90.6%	93.2%	88.5%	
	Abnormal High	2.8%	1.6%	2.5%	
WBC Count (thousand/mm^3)		(n=598)	(n=488)	(n=853)	
(continuous)[a]	--		r = 0.188		<0.001
(discrete)	Abnormal Low	14.7%	10.9%	7.2%	<0.001
	Normal	84.3%	87.3%	89.7%	
	Abnormal High	1.0%	1.8%	3.2%	
Hemoglobin (gm/dL)		(n=598)	(n=488)	(n=853)	
(continuous)	--		r = -0.033		0.142
(discrete)	Abnormal Low	12.0%	10.5%	11.6%	0.719
	Normal	87.0%	89.1%	87.7%	
	Abnormal High	1.0%	0.4%	0.7%	
Hematocrit (percent)		(n=598)	(n=488)	(n=853)	
(continuous)	--		r = -0.027		0.242
(discrete)	Abnormal Low	5.2%	3.9%	5.2%	0.863
	Normal	94.0%	95.3%	94.0%	
	Abnormal High	0.8%	0.8%	0.8%	
Platelet Count (thousand/mm^3)		(n=596)	(n=488)	(n=851)	
(continuous)[b]	--		r = 0.026		0.257
(discrete)	Abnormal Low	1.7%	2.1%	1.7%	0.126
	Normal	97.8%	97.5%	96.7%	
	Abnormal High	0.5%	0.4%	1.7%	
RBC Morphology		(n=598)	(n=488)	(n=853)	
	Abnormal	5.7%	5.3%	6.1%	0.840

Table F-8. Dependent Variable-covariate Associations for the Hematology Assessment (Continued)

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	>0–10	>10	p-Value
Absolute Neutrophils (segs) (thousand/mm^3)[b]	--		(n=1,939) r = 0.183		<0.001
Absolute Neutrophils (bands) (thousand/mm^3) (continuous)[a]	Nonzero		(n=1,557) r = 0.084		<0.001
(discrete)	Zero	(n=598) 22.2%	(n=488) 18.7%	(n=853) 18.5%	0.171
Absolute Lymphocytes (thousand/mm^3)[a]	--		(n=1,939) r = 0.049		0.030
Absolute Monocytes (thousand/mm^3)[b]	--		(n=1,939) r = 0.116		<0.001
Absolute Eosinophils (thousand/mm^3) (continuous)[a]	Nonzero		(n=1,741) r = 0.088		<0.001
(discrete)	Zero	(n=598) 11.2%	(n=488) 11.7%	(n=853) 8.7%	0.136
Absolute Basophils (thousand/mm^3) (continuous)[a]	Nonzero		(n=1,014) r = 0.068		0.030
(discrete)	Zero	(n=598) 49.3%	(n=488) 48.8%	(n=853) 46.0%	0.386
Fibrinogen (mg/dL) (continuous)[a]	--	(n=597)	(n=488) r = 0.134	(n=853)	<0.001
(discrete)	High	3.9%	5.1%	7.4%	0.014
Erythrocyte Sedimentation Rate (mm/hr) (continuous)[c]	--	(n=598)	(n=488) r = 0.100	(n=853)	<0.001
(discrete)	Abnormal	9.2%	9.4%	12.4%	0.086

Dependent Variable	Level	Body Mass Index (kg/m^2)		
		Not Obese (≤30)	Obese (>30)	p-Value
RBC Count (million/mm^3) (continuous)	--	(n=1,256) r = 0.095	(n=685)	<0.001
(discrete)	Abnormal Low	7.7%	6.4%	0.303
	Normal	90.2%	90.7%	
	Abnormal High	2.1%	2.9%	
WBC Count (thousand/mm^3) (continuous)[a]	--	(n=1,256) r = 0.076	(n=685)	<0.001
(discrete)	Abnormal Low	11.9%	7.7%	0.010
	Normal	85.8%	90.5%	
	Abnormal High	2.4%	1.8%	

Dependent Variable	Level	Body Mass Index (kg/m^2)		p-Value
		Not Obese (≤30)	Obese (>30)	
Hemoglobin (gm/dL)		(n=1,256)	(n=685)	
(continuous)	--	r = 0.011		0.634
(discrete)	Abnormal Low	11.2%	12.0%	0.715
	Normal	88.2%	87.2%	
	Abnormal High	0.6%	0.9%	
Hematocrit (percent)		(n=1,256)	(n=685)	
(continuous)	--	r = -0.012		0.600
(discrete)	Abnormal Low	4.9%	4.8%	0.982
	Normal	94.4%	94.3%	
	Abnormal High	0.8%	0.9%	
Platelet Count (thousand/mm^3)		(n=1,253)	(n=684)	
(continuous)[b]	--	r = -0.134		<0.001
(discrete)	Abnormal Low	1.4%	2.5%	0.041
	Normal	97.4%	97.1%	
	Abnormal High	1.3%	0.4%	
RBC Morphology		(n=1,256)	(n=685)	
	Abnormal	6.0%	5.4%	0.680
Absolute Neutrophils (segs)		(n=1,941)		
(thousand/mm^3)[b]	--	r = 0.043		0.056
Absolute Neutrophils (bands)				
(thousand/mm^3)		(n=1,557)		
(continuous)[a]	Nonzero	r = 0.028		0.262
(discrete)		(n=1,256)	(n=685)	
	Zero	20.2%	19.0%	0.550
Absolute Lymphocytes		(n=1,941)		
(thousand/mm^3)[a]	--	r = 0.065		0.004
Absolute Monocytes		(n=1,941)		
(thousand/mm^3)[b]	--	r = 0.072		0.002
Absolute Eosinophils				
(thousand/mm^3)		(n=1,743)		
(continuous)[a]	Nonzero	r = 0.053		0.026
(discrete)		(n=1,256)	(n=685)	
	Zero	10.0%	10.5%	0.799
Absolute Basophils				
(thousand/mm^3)		(n=1,017)		
(continuous)[a]	Nonzero	r = 0.065		0.039
(discrete)		(n=1,256)	(n=685)	
	Zero	47.9%	47.0%	0.733
Fibrinogen (mg/dL)		(n=1,255)	(n=685)	
(continuous)[a]	--	r = 0.087		<0.001
(discrete)	High	5.5%	6.1%	0.637
Erythrocyte Sedimentation Rate				
(mm/hr)		(n=1,256)	(n=685)	
(continuous)[c]	--	r = 0.112		<0.001
(discrete)	Abnormal	10.1%	11.7%	0.321

***Table F-8. Dependent Variable-covariate Associations for the Hematology Assessment
(Continued)***

[a]Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.

[b]Analysis performed on square root scale; means transformed from square root scale.

[c]Analysis performed on natural logarithm (x+0.1) scale; means transformed from natural logarithm (x+0.1) scale.

Note: Correlations (r) are based on total sample size and are not category-specific.

Please see Section 16.1.3 and Table 16-1 for a further discussion of the dependent variables and covariates shown in this appendix.

Table F-9. Dependent Variable-covariate Associations for the Renal Assessment

Dependent Variable	Level	Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
		Age			**Race**		
Occurrence of Kidney Stones	Yes	(n=888) 8.3%	(n=1,042) 12.6%	0.003	(n=125) 4.8%	(n=1,805) 11.0%	0.042
Occurrence of Kidney Disease	Yes	(n=883) 33.6%	(n=1,033) 39.7%	0.007	(n=124) 50.8%	(n=1,792) 35.9%	0.001
Blood Urea Nitrogen (mg/dL)[a]	--	(n=1,951) r = 0.241		<0.001	(n=125) O = 15.05	(n=1,826) O = 16.48	0.001
Serum Creatinine (mg/dL)[a]	--	(n=1,951) r = 0.184		<0.001	(n=125) O = 1.23	(n=1,826) O = 1.11	<0.001
Creatinine Clearance (calculated)[b]	--	(n=1,950) r = -0.538		<0.001	(n=125) O = 83.06	(n=1,825) O = 87.16	0.045
Urinary Microalbumin to Urinary Creatinine Ratio (µg/mg) (continuous – nonzero measurements)[a]	--	(n=247) r =0.230		<0.001	(n=31) O = 32.87	(n=216) O = 22.48	0.199
(discrete)	Nonzero	(n=890) 12.0%	(n=1,061) 13.2%	0.479	(n=125) 24.8%	(n=1,826) 11.8%	<0.001
Urine Specific Gravity	--	(n=1,951) r = -0.148		<0.001	(n=125) O = 1.0197	(n=1,826) O = 1.0183	0.016
Urinary Occult Blood (cells/HPF)	>2	(n=890) 2.4%	(n=1,061) 2.5%	0.999	(n=125) 5.6%	(n=1,826) 2.2%	0.035
Urinary White Blood Cell Count (cells/HPF)	>2	(n=890) 6.2%	(n=1,061) 6.1%	0.999	(n=125) 13.6%	(n=1,826) 5.6%	0.001
Urinary Protein	Present	(n=890) 3.3%	(n=1,061) 4.3%	0.265	(n=125) 8.0%	(n=1,826) 3.6%	0.024

Dependent Variable	Level	Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
		Occupation			
Occurrence of Kidney Stones	Yes	(n=759) 11.7%	(n=315) 11.4%	(n=856) 9.4%	0.265
Occurrence of Kidney Disease	Yes	(n=751) 35.7%	(n=312) 37.5%	(n=853) 37.8%	0.674
Blood Urea Nitrogen (mg/dL)[a]	--	(n=769) O = 17.22	(n=318) O = 16.25	(n=864) O = 15.73	<0.001
Serum Creatinine (mg/dL)[a]	--	(n=769) O = 1.13	(n=318) O = 1.12	(n=864) O = 1.10	0.033

| Dependent Variable | Level | Occupation | | | p-Value |
		Officer	Enlisted Flyer	Enlisted Groundcrew	
Creatinine Clearance (calculated)[b]		(n=768)	(n=318)	(n=864)	
	--	Õ = 81.70	Õ = 84.48	Õ = 92.57	<0.001
Urinary Microalbumin to Urinary Creatinine Ratio (μg/mg) (continuous – nonzero measurements)[a]		(n=76)	(n=48)	(n=123)	
	--	Õ = 25.61	Õ = 27.16	Õ = 21.21	0.548
(discrete)	Nonzero	(n=769) 9.9%	(n=318) 15.1%	(n=864) 14.2%	0.011
Urine Specific Gravity		(n=769)	(n=318)	(n=864)	
	--	Õ = 1.0173	Õ = 1.0183	Õ = 1.0194	<0.001
Urinary Occult Blood (cells/HPF)		(n=769)	(n=318)	(n=864)	
	>2	2.9%	1.6%	2.3%	0.439
Urinary White Blood Cell Count (cells/HPF)	>2	(n=769) 5.5%	(n=318) 4.4%	(n=864) 7.4%	0.096
Urinary Protein	Present	(n=769) 2.7%	(n=318) 3.8%	(n=864) 4.9%	0.082

| Dependent Variable | Level | Diabetic Class | | | p-Value |
		Normal	Impaired	Diabetic	
Occurrence of Kidney Stones	Yes	(n=1,165) 9.0%	(n=400) 14.8%	(n=365) 11.2%	0.005
Occurrence of Kidney Disease	Yes	(n=1,159) 31.6%	(n=397) 41.3%	(n=360) 49.2%	<0.001
Blood Urea Nitrogen (mg/dL)[a]		(n=1,176)	(n=406)	(n=369)	
	--	Õ = 16.02	Õ = 16.24	Õ = 17.79	<0.001
Serum Creatinine (mg/dL)[a]		(n=1,176)	(n=406)	(n=369)	
	--	Õ = 1.10	Õ = 1.13	Õ = 1.16	<0.001
Creatinine Clearance (calculated)[b]		(n=1,175)	(n=406)	(n=369)	
	--	Õ = 87.14	Õ = 86.78	Õ = 86.24	0.793
Urinary Microalbumin to Urinary Creatinine Ratio (μg/mg) (continuous – nonzero measurements)[a]		(n=108)	(n=52)	(n=87)	
	--	Õ = 16.09	Õ = 14.91	Õ = 49.83	<0.001
(discrete)	Nonzero	(n=1,176) 9.2%	(n=406) 12.8%	(n=369) 23.6%	<0.001
Urine Specific Gravity		(n=1,176)	(n=406)	(n=369)	
	--	Õ = 1.0182	Õ = 1.0183	Õ = 1.0191	0.054
Urinary Occult Blood (cells/HPF)		(n=1,176)	(n=406)	(n=369)	
	>2	2.2%	2.2%	3.3%	0.503

Dependent Variable	Level	Diabetic Class			
		Normal	Impaired	Diabetic	p-Value
Urinary White Blood Cell Count (cells/HPF)	>2	(n=1,176) 5.5%	(n=406) 7.1%	(n=369) 7.1%	0.369
Urinary Protein	Present	(n=1,176) 1.9%	(n=406) 3.5%	(n=369) 10.6%	<0.001

Dependent Variable	Level	Use of Calcium Channel Blocker at the Time of the Physical Exam			Use of ACE Inhibitor at the Time of the Physical Exam		
		No	Yes	p-Value	No	Yes	p-Value
Urinary Microalbumin to Urinary Creatinine Ratio (μg/mg) (continuous – nonzero measurements)[a]	--	(n=192) O = 19.11	(n=55) O = 49.14	<0.001	(n=160) O = 19.33	(n=87) O = 33.98	0.006
(discrete)	Nonzero	(n=1,694) 11.3%	(n=257) 21.4%	<0.001	(n=1,462) 10.9%	(n=489) 17.8%	<0.001

Dependent Variable	Level	Use of Alpha- or Beta-Adrenergic Blocking Agents at the Time of the Physical Exam			Use of Diuretics at the Time of the Physical Exam		
		No	Yes	p-Value	No	Yes	p-Value
Urinary Microalbumin to Urinary Creatinine Ratio (μg/mg) (continuous – nonzero measurements)[a]	--	(n=188) O = 19.14	(n=59) O = 45.82	<0.001	(n=197) O = 20.99	(n=50) O = 37.30	0.018
(discrete)	Nonzero	(n=1,535) 12.3%	(n=416) 14.2%	0.332	(n=1,689) 11.7%	(n=262) 19.1%	0.001

[a]Analysis was performed on natural logarithm scale; means were transformed from natural logarithm scale.
[b]Analysis was performed on square root scale; means were transformed from square root scale.

Note: Correlation coefficients (r) are based on total sample size and are not category-specific.

Please see Section 17.1.3 and Table 17-1 for a further discussion of the dependent variables and covariates shown in this appendix.

Table F-10. Dependent Variable-covariate Associations for the Endocrinology Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Past Thyroid Disease		(n=887)	(n=1,050)		(n=125)	(n=1,812)	
	Yes	10.6%	13.4%	0.067	8.0%	12.4%	0.186
Composite Diabetes Indicator: 2002 AFHS Diabetes Definition		(n=890)	(n=1,059)		(n=125)	(n=1,824)	
	Diabetic	12.9%	23.8%	<0.001	28.8%	18.2%	0.005
Composite Diabetes Indicator: pre-2002 AFHS Diabetes Definition		(n=890)	(n=1,059)		(n=125)	(n=1,824)	
	Diabetic	15.1%	26.9%	<0.001	31.2%	20.8%	0.009
Diabetic Control: 2002 AFHS Diabetes Definition		(n=890)	(n=1,059)		(n=125)	(n=1,824)	
	Nondiabetic	87.1%	76.2%	<0.001	71.2%	81.9%	0.012
	No Treatment	2.8%	3.7%		3.2%	3.3%	
	Diet and Exercise	1.7%	3.9%		3.2%	2.9%	
	Oral Hypoglycemics	6.5%	13.1%		19.2%	9.5%	
	Requiring Insulin	1.9%	3.1%		3.2%	2.5%	
Diabetic Control: pre-2002 AFHS Diabetes Definition		(n=890)	(n=1,059)		(n=125)	(n=1,824)	
	Nondiabetic	84.9%	73.1%	<0.001	68.8%	79.2%	0.012
	No Treatment	4.9%	6.7%		5.6%	5.9%	
	Diet and Exercise	1.7%	4.0%		3.2%	2.9%	
	Oral Hypoglycemics	6.5%	13.1%		19.2%	9.5%	
	Requiring Insulin	1.9%	3.1%		3.2%	2.5%	
Time to Diabetes Onset: 2002 AFHS Diabetes Definition (years)		(n=890)	(n=1,059)		(n=125)	(n=1,824)	
		32.08[a]	25.09[a]	<0.001	24.17[a]	28.67[a]	0.002
Time to Diabetes Onset: pre-2002 AFHS Diabetes Definition (years)		(n=890)	(n=1,059)		(n=125)	(n=1,824)	
		31.75[a]	25.09[a]	<0.001	24.17[a]	28.67[a]	0.003
Thyroid Gland		(n=852)	(n=975)		(n=123)	(n=1,704)	
	Abnormal	1.8%	1.7%	0.999	2.4%	1.7%	0.806
Testicular Examination		(n=884)	(n=1,038)		(n=123)	(n=1,799)	
	Abnormal	3.3%	10.1%	<0.001	7.3%	7.0%	0.999
TSH (μIU/mL)		(n=851)	(n=971)		(n=123)	(n=1,699)	
(continuous)[b]	--	r = 0.101		<0.001	O = 1.389	O = 1.795	<0.001
(discrete)	Abnormal Low	0.2%	0.6%	0.256	0.0%	0.5%	0.144
	Normal	97.8%	96.6%		100.0%	96.9%	
	Abnormal High	2.0%	2.8%		0.0%	2.6%	
Free T$_4$ (ng/dL)		(n=851)	(n=971)		(n=123)	(n=1,699)	
(continuous)[b]	--	r = 0.038		0.101	O = 1.068	O = 1.070	0.862
(discrete)	Low	9.5%	10.2%	0.686	9.8%	9.9%	0.999
Anti-thyroid Antibodies		(n=851)	(n=971)		(n=123)	(n=1,699)	
	Present	0.7%	0.4%	0.598	0.0%	0.6%	0.825

Table F-10. Dependent Variable-covariate Associations for the Endocrinology Assessment (Continued)

Dependent Variable	Level	Age Born ≥1942	Age Born <1942	p-Value	Race Black	Race Non-Black	p-Value
Fasting Glucose (mg/dL)		(n=890)	(n=1,059)		(n=125)	(n=1,824)	
(continuous)[b]	--	r = 0.081		<0.001	O = 108.1	O = 101.5	0.001
(discrete)	High	15.4%	24.8%	<0.001	25.6%	20.2%	0.181
2-hour Postprandial Glucose (mg/dL)[c]		(n=770)	(n=795)		(n=89)	(n=1,476)	
(continuous)[b]	--	r = 0.186		<0.001	O = 111.5	O = 106.9	0.249
(discrete)	Impaired	15.7%	26.4%	<0.001	21.4%	21.1%	0.999
2-hour Postprandial Urinary Glucose[c]		(n=770)	(n=795)		(n=89)	(n=1,476)	
	Present	27.1%	25.7%	0.543	19.1%	26.8%	0.138
Fasting Insulin (μIU/mL)		(n=890)	(n=1,059)		(n=125)	(n=1,824)	
(continuous)[b]	--	r = -0.057		0.011	O = 11.15	O = 10.93	0.714
(discrete)	Abnormal Low	9.4%	9.1%	0.031	9.6%	9.2%	0.988
	Normal	82.7%	85.9%		84.0%	84.5%	
	Abnormal High	7.9%	5.0%		6.4%	6.3%	
2-hour Postprandial Insulin (μIU/mL)[c]		(n=770)	(n=795)		(n=89)	(n=1,476)	
(continuous)[b]	--	r = 0.020		0.421	O = 68.54	O = 57.84	0.045
(discrete)	Abnormal Low	5.7%	4.5%	0.471	3.4%	5.2%	0.020
	Normal	45.7%	44.8%		32.6%	46.0%	
	Abnormal High	48.6%	50.7%		64.0%	48.8%	
Hemoglobin A1c (percent)[d]		(n=114)	(n=246)		(n=36)	(n=324)	
(continuous)[b]	--	r = -0.131		0.013	O = 7.34	O = 6.61	0.002
(discrete)	High	69.3%	63.8%	0.369	75.0%	64.5%	0.284
C-peptide (ng/mL)[d]		(n=114)	(n=246)		(n=36)	(n=324)	
(continuous)[e]	--	r = -0.021		0.696	O = 3.05	O = 3.87	0.008
(discrete)	High	30.7%	23.2%	0.163	8.3%	27.5%	0.022
Proinsulin (pmol/L)[d]		(n=114)	(n=246)		(n=36)	(n=324)	
(continuous)[b]	--	r = -0.122		0.021	O = 20.03	O = 24.23	0.346
(discrete)	High	60.5%	43.9%	0.005	41.7%	50.0%	0.440
GADA[d]		(n=114)	(n=246)		(n=36)	(n=324)	
	Present	2.6%	3.7%	0.850	0.0%	3.7%	0.493
Total Testosterone (ng/dL)		(n=883)	(n=1,048)		(n=125)	(n=1,806)	
(continuous)[e]	--	r = -0.105		<0.001	O = 415.4	O = 408.1	0.685
(discrete)	Low	12.6%	17.4%	0.004	14.4%	15.2%	0.904
Free Testosterone (pg/dL)		(n=883)	(n=1,048)		(n=125)	(n=1,806)	
(continuous)[e]	--	r = -0.294		<0.001	O = 10.67	O = 10.43	0.505
(discrete)	Low	3.2%	8.1%	<0.001	6.4%	5.8%	0.942

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Estradiol (pg/mL) (continuous – measurements above sensitivity limit)[b]	--	(n=1,249) r = 0.018		0.531	(n=97) O = 25.30	(n=1,152) O = 21.54	0.003
(discrete – all observations)	High	(n=883) 2.3%	(n=1,048) 3.2%	0.296	(n=125) 3.2%	(n=1,806) 2.7%	0.969
LH (mIU/mL)		(n=883)	(n=1,048)		(n=125)	(n=1,806)	
(continuous)[b]	--	r = 0.216		<0.001	O = 4.35	O = 4.44	0.716
(discrete)	High	2.8%	7.5%	<0.001	3.2%	5.5%	0.360
FSH (mIU/mL)		(n=883)	(n=1,048)		(n=125)	(n=1,806)	
(continuous)[b]	--	r = 0.267		<0.001	O = 5.39	O = 5.74	0.317
(discrete)	High	2.2%	9.1%	<0.001	5.6%	5.9%	0.999

Dependent Variable	Level	Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Past Thyroid Disease		(n=763)	(n=317)	(n=857)	
	Yes	12.6%	12.0%	11.8%	0.884
Composite Diabetes Indicator: 2002 AFHS Diabetes Definition		(n=768)	(n=318)	(n=863)	
	Diabetic	16.8%	22.6%	19.2%	0.075
Composite Diabetes Indicator: pre-2002 AFHS Diabetes Definition		(n=768)	(n=318)	(n=863)	
	Diabetic	19.0%	25.8%	22.1%	0.039
Diabetic Control: 2002 AFHS Diabetes Definition		(n=768)	(n=318)	(n=863)	
	Nondiabetic	83.2%	77.4%	80.8%	0.579
	No Treatment	2.9%	3.8%	3.5%	
	Diet and Exercise	2.7%	4.1%	2.6%	
	Oral Hypoglycemics	8.7%	12.0%	10.7%	
	Requiring Insulin	2.5%	2.8%	2.6%	
Diabetic Control: pre-2002 AFHS Diabetes Definition		(n=768)	(n=318)	(n=863)	
	Nondiabetic	81.0%	74.2%	77.9%	0.409
	No Treatment	5.0%	6.9%	6.4%	
	Diet and Exercise	2.9%	4.1%	2.6%	
	Oral Hypoglycemics	8.7%	12.0%	10.7%	
	Requiring Insulin	2.5%	2.8%	2.6%	
Time to Diabetes Onset: 2002 AFHS Diabetes Definition (years)		(n=768) 28.08[a]	(n=318) 27.08[a]	(n=863) 28.67[a]	0.100
Time to Diabetes Onset: pre-2002 AFHS Diabetes Definition (years)		(n=768) 28.08[a]	(n=318) 27.08[a]	(n=863) 28.67[a]	0.065
Thyroid Gland		(n=707)	(n=300)	(n=820)	
	Abnormal	1.6%	1.0%	2.2%	0.354

Dependent Variable	Level	Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
				Occupation	
Testicular Examination		(n=755)	(n=312)	(n=855)	
	Abnormal	7.3%	8.7%	6.1%	0.284
TSH (µIU/mL)		(n=703)	(n=300)	(n=819)	
(continuous)[b]	--	O = 1.885	O = 1.753	O = 1.670	<0.001
(discrete)	Abnormal Low	0.4%	0.7%	0.4%	0.726
	Normal	96.6%	97.3%	97.6%	
	Abnormal High	3.0%	2.0%	2.1%	
Free T_4 (ng/dL)		(n=703)	(n=300)	(n=819)	
(continuous)[b]	--	O = 1.073	O = 1.080	O = 1.064	0.339
(discrete)	Low	9.3%	10.3%	10.3%	0.772
Anti-thyroid Antibodies		(n=703)	(n=300)	(n=819)	
	Present	0.7%	1.0%	0.2%	0.240
Fasting Glucose (mg/dL)		(n=768)	(n=318)	(n=863)	
(continuous)[b]	--	O = 100.5	O = 103.3	O = 102.7	0.046
(discrete)	High	18.9%	23.3%	21.0%	0.241
2-hour Postprandial Glucose (mg/dL)[c]		(n=632)	(n=242)	(n=691)	
(continuous)[b]	--	O = 106.7	O = 114.8	O = 105.0	0.002
(discrete)	Impaired	18.8%	27.7%	21.0%	0.016
2-hour Postprandial Urinary Glucose[c]		(n=632)	(n=242)	(n=691)	
	Present	20.1%	32.2%	30.1%	<0.001
Fasting Insulin (µIU/mL)		(n=768)	(n=318)	(n=863)	
(continuous)[b]	--	O = 10.06	O = 11.35	O = 11.65	<0.001
(discrete)	Abnormal Low	11.2%	7.6%	8.1%	0.021
	Normal	84.1%	86.2%	84.1%	
	Abnormal High	4.7%	6.3%	7.8%	
2-hour Postprandial Insulin (µIU/mL)[c]		(n=632)	(n=242)	(n=691)	
(continuous)[b]	--	O = 52.16	O = 66.62	O = 61.85	<0.001
(discrete)	Abnormal Low	6.0%	2.9%	5.1%	<0.001
	Normal	51.3%	40.1%	41.5%	
	Abnormal High	42.7%	57.0%	53.4%	
Hemoglobin A1c (percent)[d]		(n=126)	(n=70)	(n=164)	
(continuous)[b]	--	O = 6.39	O = 6.71	O = 6.89	0.004
(discrete)	High	56.4%	67.1%	72.0%	0.021
C-peptide (ng/mL)[d]		(n=126)	(n=70)	(n=164)	
(continuous)[e]	--	O = 3.79	O = 3.70	O = 3.80	0.926
(discrete)	High	23.0%	22.9%	28.7%	0.467
Proinsulin (pmol/L)[d]		(n=126)	(n=70)	(n=164)	
(continuous)[b]	--	O = 20.72	O = 25.06	O = 25.84	0.247
(discrete)	High	42.1%	50.0%	54.3%	0.118

Dependent Variable	Level	Occupation			p-Value
		Officer	**Enlisted Flyer**	**Enlisted Groundcrew**	
GADA[d]		(n=126)	(n=70)	(n=164)	
	Present	4.0%	2.9%	3.1%	0.883
Total Testosterone (ng/dL)		(n=760)	(n=314)	(n=857)	
(continuous)[e]	--	O = 397.9	O = 415.7	O = 415.6	0.142
(discrete)	Low	15.4%	14.7%	15.2%	0.953
Free Testosterone (pg/dL)		(n=760)	(n=314)	(n=857)	
(continuous)[e]	--	O = 9.92	O = 10.26	O = 10.99	<0.001
(discrete)	Low	6.7%	8.3%	4.2%	0.013
Estradiol (pg/mL)		(n=486)	(n=208)	(n=555)	
(continuous – measurements above sensitivity limit)[b]	--	O = 21.78	O = 22.22	O = 21.70	0.847
(discrete – all measurements)		(n=760)	(n=314)	(n=857)	
	High	2.8%	3.2%	2.6%	0.848
LH (mIU/mL)		(n=760)	(n=314)	(n=857)	
(continuous)[b]	--	O = 4.55	O = 4.51	O = 4.31	0.217
(discrete)	High	5.7%	5.7%	5.0%	0.814
FSH (mIU/mL)		(n=760)	(n=314)	(n=857)	
(continuous)[b]	--	O = 6.06	O = 5.69	O = 5.44	0.007
(discrete)	High	7.8%	7.6%	3.6%	<0.001

Dependent Variable	Level	Body Mass Index (kg/m^2)		p-Value
		Not Obese (≤30)	**Obese (>30)**	
Past Thyroid Disease		(n=1,253)	(n=683)	
	Yes	11.3%	13.8%	0.123
Composite Diabetes Indicator: 2002 AFHS Diabetes Definition		(n=1,259)	(n=689)	
	Diabetic	14.2%	27.3%	<0.001
Composite Diabetes Indicator: pre-2002 AFHS Diabetes Definition		(n=1,259)	(n=689)	
	Diabetic	16.0%	31.5%	<0.001
Diabetic Control: 2002 AFHS Diabetes Definition		(n=1,259)	(n=689)	
	Nondiabetic	85.8%	72.7%	<0.001
	No Treatment	2.1%	5.5%	
	Diet and Exercise	3.0%	2.6%	
	Oral Hypoglycemics	7.2%	15.5%	
	Requiring Insulin	2.0%	3.6%	
Diabetic Control: pre-2002 AFHS Diabetes Definition		(n=1,259)	(n=689)	
	Nondiabetic	84.0%	68.5%	<0.001
	No Treatment	3.8%	9.7%	
	Diet and Exercise	3.1%	2.6%	
	Oral Hypoglycemics	7.2%	15.5%	
	Requiring Insulin	2.0%	3.6%	
Time to Diabetes Onset: 2002 AFHS Diabetes Definition (years)		(n=1,259)	(n=689)	
		30.83[a]	25.83[a]	<0.001

Table F-10. Dependent Variable-covariate Associations for the Endocrinology Assessment (Continued)

Dependent Variable	Level	Body Mass Index (kg/m^2)		
		Not Obese (≤30)	Obese (>30)	p-Value
Time to Diabetes Onset: pre-2002 AFHS Diabetes Definition (years)		(n=1,259) 30.83[a]	(n=689) 25.83[a]	<0.001
Thyroid Gland		(n=1,184)	(n=643)	
	Abnormal	1.7%	1.9%	0.929
Testicular Examination		(n=1,245)	(n=677)	
	Abnormal	7.4%	6.2%	0.378
TSH (μIU/mL)		(n=1,179)	(n=642)	
(continuous)[b]	--	r = 0.040		0.086
(discrete)	Abnormal Low	0.4%	0.5%	0.532
	Normal	97.5%	96.6%	
	Abnormal High	2.1%	3.0%	
Free T$_4$ (ng/dL)		(n=1,179)	(n=642)	
(continuous)[b]	--	r = -0.110		<0.001
(discrete)	Low	8.4%	12.6%	0.005
Anti-thyroid Antibodies		(n=1,179)	(n=642)	
	Present	0.5%	0.6%	0.999
Fasting Glucose (mg/dL)		(n=1,259)	(n=689)	
(continuous)[b]	--	r = 0.229		<0.001
(discrete)	High	15.5%	29.8%	<0.001
2-hour Postprandial Glucose (mg/dL)[c]		(n=1,070)	(n=494)	
(continuous)[b]	--	r = 0.232		<0.001
(discrete)	Impaired	16.9%	30.4%	<0.001
2-hour Postprandial Urinary Glucose[c]		(n=1,070)	(n=494)	
	Present	25.3%	28.7%	0.173
Fasting Insulin (μIU/mL)		(n=1,259)	(n=689)	
(continuous)[b]	--	r = 0.492		<0.001
(discrete)	Abnormal Low	13.2%	2.0%	<0.001
	Normal	84.0%	85.3%	
	Abnormal High	2.9%	12.6%	
2-hour Postprandial Insulin (μIU/mL)[c]		(n=1,070)	(n=494)	
(continuous)[b]	--	r = 0.395		<0.001
(discrete)	Abnormal Low	6.6%	1.8%	<0.001
	Normal	53.1%	28.1%	
	Abnormal High	40.3%	70.0%	
Hemoglobin A1c (percent)[d]		(n=176)	(n=184)	
(continuous)[b]	--	r = -0.024		0.647
(discrete)	High	61.4%	69.6%	0.127
C-peptide (ng/mL)[d]		(n=176)	(n=184)	
(continuous)[e]	--	r = 0.349		<0.001
(discrete)	High	13.1%	37.5%	<0.001
Proinsulin (pmol/L)[d]		(n=176)	(n=184)	
(continuous)[b]	--	r = 0.339		<0.001
(discrete)	High	31.8%	65.8%	<0.001

Dependent Variable	Level	Body Mass Index (kg/m^2)		
		Not Obese (≤30)	Obese (>30)	p-Value
GADA[d]		(n=176)	(n=184)	
	Present	3.4%	3.3%	0.999
Total Testosterone (ng/dL)		(n=1,247)	(n=683)	
(continuous)[e]	--	r = -0.376		<0.001
(discrete)	Low	10.2%	24.2%	<0.001
Free Testosterone (pg/dL)		(n=1,247)	(n=683)	
(continuous)[e]	--	r = -0.264		<0.001
(discrete)	Low	4.1%	8.9%	<0.001
Estradiol (pg/mL)		(n=1,249)		
(continuous – measurements above sensitivity limit)[b]	--	r = 0.010		0.729
(discrete – all measurements)		(n=1,247)	(n=683)	
	High	2.3%	3.5%	0.167
LH (mIU/mL)		(n=1,247)	(n=683)	
(continuous)[b]	--	r = -0.036		0.116
(discrete)	High	5.8%	4.7%	0.364
FSH (mIU/mL)		(n=1,247)	(n=683)	
(continuous)[b]	--	r = -0.018		0.435
(discrete)	High	6.1%	5.6%	0.710

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	>0-10	>10	p-Value
Composite Diabetes Indicator: 2002 AFHS Diabetes Definition	Diabetic	(n=600)	(n=491)	(n=855)	
		16.2%	15.1%	22.8%	<0.001
Composite Diabetes Indicator: pre-2002 AFHS Diabetes Definition	Diabetic	(n=600)	(n=491)	(n=855)	
		19.2%	17.5%	25.4%	<0.001
Diabetic Control: 2002 AFHS Diabetes Definition		(n=600)	(n=491)	(n=855)	
	Nondiabetic	83.8%	84.9%	77.2%	0.004
	No Treatment	3.3%	3.1%	3.4%	
	Diet and Exercise	3.0%	2.0%	3.3%	
	Oral Hypoglycemics	8.7%	7.9%	12.4%	
	Requiring Insulin	1.2%	2.0%	3.7%	
Diabetic Control: pre-2002 AFHS Diabetes Definition		(n=600)	(n=491)	(n=855)	
	Nondiabetic	80.8%	82.5%	74.6%	0.004
	No Treatment	6.2%	5.5%	6.0%	
	Diet and Exercise	3.2%	2.0%	3.3%	
	Oral Hypoglycemics	8.7%	7.9%	12.4%	
	Requiring Insulin	1.2%	2.0%	3.7%	
Time to Diabetes Onset: 2002 AFHS Diabetes Definition (years)		(n=600)	(n=491)	(n=855)	
		29.83[a]	29.92[a]	25.83[a]	<0.001
Time to Diabetes Onset: pre-2002 AFHS Diabetes Definition (years)		(n=600)	(n=491)	(n=855)	
		29.83[a]	29.92[a]	25.83[a]	<0.001

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	>0-10	>10	p-Value
Fasting Glucose (mg/dL)		(n=600)	(n=491)	(n=855)	
(continuous)[b]	--		r = 0.068		0.003
(discrete)	High	18.8%	16.1%	24.2%	<0.001
2-hour Postprandial Glucose (mg/dL)[c]		(n=500)	(n=411)	(n=652)	
(continuous)[b]	--		r = 0.041		0.103
(discrete)	Impaired	20.6%	18.0%	23.6%	0.086
2-hour Postprandial Urinary Glucose[c]		(n=500)	(n=411)	(n=652)	
	Present	24.2%	25.8%	28.5%	0.242
Fasting Insulin (μIU/mL)		(n=600)	(n=491)	(n=855)	
(continuous)[b]	--		r = 0.069		0.002
(discrete)	Abnormal Low	9.5%	10.6%	8.3%	0.262
	Normal	84.8%	84.3%	84.2%	
	Abnormal High	5.7%	5.1%	7.5%	
2-hour Postprandial Insulin (μIU/mL)[c]		(n=500)	(n=411)	(n=652)	
(continuous)[b]	--		r = 0.034		0.175
(discrete)	Abnormal Low	4.6%	8.0%	3.7%	0.024
	Normal	46.2%	45.3%	44.5%	
	Abnormal High	49.2%	46.7%	51.8%	
Hemoglobin A1c (percent)[d]		(n=97)	(n=71)	(n=191)	
(continuous)[b]	--		r = -0.019		0.723
(discrete)	High	62.9%	76.1%	62.8%	0.111
C-peptide (ng/mL)[d]		(n=97)	(n=71)	(n=191)	
(continuous)[e]	--		r = 0.105		0.047
(discrete)	High	16.5%	22.5%	31.4%	0.019
Proinsulin (pmol/L)[d]		(n=97)	(n=71)	(n=191)	
(continuous)[b]	--		r = 0.027		0.610
(discrete)	High	42.3%	54.9%	50.8%	0.225
GADA[d]		(n=97)	(n=71)	(n=191)	
	Present	3.1%	2.8%	3.7%	0.932

Dependent Variable	Level	Waist-to-hip Ratio		
		≤1	>1	p-Value
Composite Diabetes Indicator: 2002 AFHS Diabetes Definition		(n=992)	(n=955)	
	Diabetic	11.8%	26.1%	<0.001
Composite Diabetes Indicator: pre-2002 AFHS Diabetes Definition		(n=992)	(n=955)	
	Diabetic	13.8%	29.4%	<0.001
Diabetic Control: 2002 AFHS Diabetes Definition		(n=992)	(n=955)	
	Nondiabetic	88.2%	73.9%	<0.001
	No Treatment	2.6%	4.0%	
	Diet and Exercise	2.2%	3.6%	
	Oral Hypoglycemics	5.1%	15.2%	
	Requiring Insulin	1.8%	3.4%	

Dependent Variable	Level	Waist-to-hip Ratio		p-Value
		≤1	>1	
Diabetic Control: pre-2002 AFHS Diabetes Definition		(n=992)	(n=955)	
	Nondiabetic	86.2%	70.6%	<0.001
	No Treatment	4.6%	7.2%	
	Diet and Exercise	2.2%	3.7%	
	Oral Hypoglycemics	5.1%	15.2%	
	Requiring Insulin	1.8%	3.4%	
Time to Diabetes Onset: 2002 AFHS Diabetes Definition (years)		(n=992)	(n=955)	
		32.50[a]	24.92[a]	<0.001
Time to Diabetes Onset: pre-2002 AFHS Diabetes Definition (years)		(n=992)	(n=955)	
		32.08[a]	24.92[a]	<0.001
Fasting Glucose (mg/dL)		(n=992)	(n=955)	
(continuous)[b]	--	r = 0.199		<0.001
(discrete)	High	12.7%	28.6%	<0.001
2-hour Postprandial Glucose (mg/dL)[c]		(n=866)	(n=698)	
(continuous)[b]	--	r = 0.213		<0.001
(discrete)	Impaired	15.7%	27.9%	<0.001
2-hour Postprandial Urinary Glucose[c]		(n=866)	(n=698)	
	Present	23.0%	30.7%	<0.001
Fasting Insulin (μIU/mL)		(n=992)	(n=955)	
(continuous)[b]	--	r = 0.323		<0.001
(discrete)	Abnormal Low	13.9%	4.4%	<0.001
	Normal	82.9%	86.1%	
	Abnormal High	3.2%	9.5%	
2-hour Postprandial Insulin (μIU/mL)[c]		(n=866)	(n=698)	
(continuous)[b]	--	r = 0.314		<0.001
(discrete)	Abnormal Low	7.6%	2.0%	<0.001
	Normal	53.4%	35.1%	
	Abnormal High	39.0%	62.9%	
Hemoglobin A1c (percent)[d]		(n=116)	(n=243)	
(continuous)[b]	--	r = -0.028		0.601
(discrete)	High	64.7%	65.8%	0.918
C-peptide (ng/mL)[d]		(n=116)	(n=243)	
(continuous)[e]	--	r = 0.241		<0.001
(discrete)	High	14.7%	30.5%	0.002
Proinsulin (pmol/L)[d]		(n=116)	(n=243)	
(continuous)[e]	--	r = 0.288		<0.001
(discrete)	High	37.9%	54.3%	0.005
GADA[d]		(n=116)	(n=243)	
	Present	2.6%	3.7%	0.813

Dependent Variable	Level	Family History of Diabetes		
		Yes	No	p-Value
Composite Diabetes Indicator: 2002 AFHS Diabetes Definition	Diabetic	(n=613) 27.2%	(n=1,319) 14.6%	<0.001
Composite Diabetes Indicator: pre-2002 AFHS Diabetes Definition	Diabetic	(n=613) 30.0%	(n=1,319) 17.2%	<0.001
Diabetic Control: 2002 AFHS Diabetes Definition	Nondiabetic No Treatment Diet and Exercise Oral Hypoglycemics Requiring Insulin	(n=613) 72.8% 5.2% 3.9% 14.7% 3.4%	(n=1,319) 85.4% 2.4% 2.3% 7.9% 2.0%	<0.001
Diabetic Control: pre-2002 AFHS Diabetes Definition	Nondiabetic No Treatment Diet and Exercise Oral Hypoglycemics Requiring Insulin	(n=613) 70.0% 7.8% 4.1% 14.7% 3.4%	(n=1,319) 82.8% 5.1% 2.3% 7.9% 2.0%	<0.001
Time to Diabetes Onset: 2002 AFHS Diabetes Definition (years)		(n=613) 24.08[a]	(n=1,319) 30.42[a]	<0.001
Time to Diabetes Onset: pre-2002 AFHS Diabetes Definition (years)		(n=613) 24.08[a]	(n=1,319) 30.42[a]	<0.001
Fasting Glucose (mg/dL)		(n=613)	(n=1,319)	
(continuous)[b] (discrete)	-- High	O = 106.7 27.4%	O = 99.7 17.2%	<0.001 <0.001
2-hour Postprandial Glucose (mg/dL)[c]		(n=440)	(n=1,116)	
(continuous)[b] (discrete)	-- Impaired	O = 111.2 24.6%	O = 105.8 19.9%	0.008 0.051
2-hour Postprandial Urinary Glucose[c]	Present	(n=440) 27.1%	(n=1,116) 26.2%	0.771
Fasting Insulin (μIU/mL)		(n=613)	(n=1,319)	
(continuous)[b] (discrete)	-- Abnormal Low Normal Abnormal High	O = 11.81 7.8% 83.9% 8.3%	O = 10.57 9.9% 84.7% 5.4%	<0.001 0.021
2-hour Postprandial Insulin (μIU/mL)[c]		(n=440)	(n=1,116)	
(continuous)[b] (discrete)	-- Abnormal Low Normal Abnormal High	O = 64.33 3.2% 41.4% 55.5%	O = 56.21 5.9% 46.7% 47.4%	0.002 0.005
Hemoglobin A1c (percent)[d]		(n=166)	(n=186)	
(continuous)[b] (discrete)	-- High	O = 6.77 70.5%	O = 6.61 61.8%	0.236 0.110

Table F-10. Dependent Variable-covariate Associations for the Endocrinology Assessment (Continued)

Dependent Variable	Level	Family History of Diabetes		
		Yes	No	p-Value
C-peptide (ng/mL)[d]		(n=166)	(n=186)	
(continuous)[e]	--	$O = 3.62$	$O = 3.94$	0.100
(discrete)	High	22.3%	29.0%	0.187
Proinsulin (pmol/L)[d]		(n=166)	(n=186)	
(continuous)[b]	--	$O = 22.76$	$O = 25.08$	0.433
(discrete)	High	50.0%	49.5%	0.999
GADA[d]		(n=166)	(n=186)	
	Present	3.6%	3.2%	0.999

[a] 10th percentile of distribution of time to onset of diabetes. For diabetics, time to diabetes onset was determined as the difference between the date on which a participant was first diagnosed with diabetes and the end date of the last qualifying tour of duty in SEA. For nondiabetics, time to diabetes onset was determined as the difference between the date of the participant's 2002 physical examination and the end date of the last qualifying tour of duty in SEA.

[b] Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.

[c] Data was collected for nondiabetics only.

[d] Data was collected for diabetics only.

[e] Analysis performed on square root scale; means transformed from square root scale.

Note: Correlations (r) are based on total sample size and are not category-specific.

Please see Section 18.1.3 and Table 18-1 for a further discussion of the dependent variables and covariates shown in this appendix.

Table F-11. Dependent Variable-covariate Associations for the Immunology Assessment

Dependent Variable	Level	Age Born ≥1942	Born <1942	p-Value	Race Black	Non-Black	p-Value
CD3+ Cells (T Cells) (cells/mm^3)^a		(n=694)			(n=43)	(n=651)	
	--	r = -0.150		<0.001	O = 1,345.5	O = 1,207.1	0.082
CD4+ Cells (Helper T Cells) (cells/mm^3)^b		(n=694)			(n=43)	(n=651)	
	--	r = -0.202		<0.001	O = 1,000.7	O = 870.5	0.019
CD8+ Cells (Suppressor Cells) (cells/mm^3)^a		(n=694)			(n=43)	(n=651)	
	--	r = 0.036		0.346	O = 588.4	O = 517.1	0.090
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)^a		(n=694)			(n=43)	(n=651)	
	--	r = 0.119		0.002	O = 232.9	O = 222.5	0.583
CD20+ Cells (B Cells) (cells/mm^3)^a		(n=694)			(n=43)	(n=651)	
	--	r = -0.271		<0.001	O = 235.0	O = 183.3	0.015
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)^b		(n=694)			(n=43)	(n=651)	
	--	r = -0.209		<0.001	O = 918.8	O = 803.7	0.030
Absolute Lymphocytes (cells/mm^3)^a		(n=1,763)			(n=115)	(n=1,648)	
	--	r = -0.119		<0.001	O = 1,744.2	O = 1,651.9	0.159
IgA (mg/dL)^b		(n=1,763)			(n=115)	(n=1,648)	
	--	r = 0.041		0.087	O = 291.9	O = 254.5	0.002
IgG (mg/dL)^a		(n=1,763)			(n=115)	(n=1,648)	
	--	r = -0.004		0.875	O = 1,300.5	O = 1,043.0	<0.001
IgM (mg/dL)^a		(n=1,763)			(n=115)	(n=1,648)	
	--	r = -0.091		<0.001	O = 80.54	O = 91.24	0.034
Lupus Panel: ANA Test		(n=826)	(n=937)		(n=115)	(n=1,648)	
	Present	16.1%	21.8%	0.003	10.4%	19.7%	0.020
Lupus Panel: Thyroid Microsomal Antibody		(n=826)	(n=937)		(n=115)	(n=1,648)	
	Present	3.0%	2.4%	0.463	0.9%	2.8%	0.349
Lupus Panel: MSK Anti-smooth Muscle Antibody		(n=826)	(n=937)		(n=115)	(n=1,648)	
	Present	0.9%	1.1%	0.820	3.5%	0.8%	0.018
Lupus Panel: MSK Anti-mitochondrial Antibody		(n=826)	(n=937)		(n=115)	(n=1,648)	
	Present	0.2%	0.2%	0.999	0.0%	0.2%	0.999
Lupus Panel: MSK Anti-parietal Cell Antibody		(n=826)	(n=937)		(n=115)	(n=1,648)	
	Present	2.5%	3.0%	0.672	2.6%	2.8%	0.999
Lupus Panel: Rheumatoid Factor		(n=826)	(n=937)		(n=115)	(n=1,648)	
	Present	20.9%	22.3%	0.526	28.7%	21.2%	0.076

		Occupation			
Dependent Variable	Level	Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
CD3+ Cells (T Cells) (cells/mm^3)[a]		(n=267)	(n=123)	(n=304)	
	--	O = 1,147.0	O = 1,211.5	O = 1,280.1	0.004
CD4+ Cells (Helper T Cells) (cells/mm^3)[b]		(n=267)	(n=123)	(n=304)	
	--	O = 838.4	O = 862.3	O = 920.7	0.013
CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]		(n=267)	(n=123)	(n=304)	
	--	O = 490.7	O = 553.4	O = 536.5	0.028
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]		(n=267)	(n=123)	(n=304)	
	--	O = 218.2	O = 235.3	O = 222.7	0.423
CD20+ Cells (B Cells) (cells/mm^3)[a]		(n=267)	(n=123)	(n=304)	
	--	O = 164.5	O = 179.5	O = 210.6	<0.001
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[b]		(n=267)	(n=123)	(n=304)	
	--	O = 771.9	O = 795.7	O = 851.5	0.012
Absolute Lymphocytes (cells/mm^3)[a]		(n=693)	(n=283)	(n=787)	
	--	O = 1,546.9	O = 1,664.5	O = 1,759.3	<0.001
IgA (mg/dL)[b]		(n=693)	(n=283)	(n=787)	
	--	O = 247.7	O = 257.5	O = 264.9	0.024
IgG (mg/dL)[a]		(n=693)	(n=283)	(n=787)	
	--	O = 1,027.4	O = 1,068.9	O = 1,081.8	<0.001
IgM (mg/dL)[a]		(n=693)	(n=283)	(n=787)	
	--	O = 87.00	O = 91.83	O = 93.22	0.086
Lupus Panel: ANA Test		(n=693)	(n=283)	(n=787)	
	Present	20.2%	17.0%	18.9%	0.498
Lupus Panel: Thyroid Microsomal Antibody		(n=693)	(n=283)	(n=787)	
	Present	2.7%	2.1%	2.8%	0.822
Lupus Panel: MSK Anti-smooth Muscle Antibody		(n=693)	(n=283)	(n=787)	
	Present	1.2%	1.4%	0.6%	0.417
Lupus Panel: MSK Anti-mitochondrial Antibody		(n=693)	(n=283)	(n=787)	
	Present	0.4%	0.4%	0.0%	0.193
Lupus Panel: MSK Anti-parietal Cell Antibody		(n=693)	(n=283)	(n=787)	
	Present	2.2%	2.1%	3.6%	0.203
Lupus Panel: Rheumatoid Factor		(n=693)	(n=283)	(n=787)	
	Present	18.6%	25.4%	23.0%	0.030

Dependent Variable	Level	Body Mass Index (kg/m^2)		p-Value
		Not Obese (≤30)	Obese (>30)	
CD3+ Cells (T Cells) (cells/mm^3)[a]		(n=694)		
	--	r = 0.058		0.125
CD4+ Cells (Helper T Cells) (cells/mm^3)[b]		(n=694)		
	--	r = 0.057		0.132
CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]		(n=694)		
	--	r = 0.029		0.438
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]		(n=694)		
	--	r = 0.074		0.051
CD20+ Cells (B Cells) (cells/mm^3)[a]		(n=694)		
	--	r = 0.079		0.038
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[b]		(n=694)		
	--	r = 0.052		0.171
Absolute Lymphocytes (cells/mm^3)[a]		(n=1,762)		
	--	r = 0.069		0.004
IgA (mg/dL)[b]		(n=1,762)		
	--	r = 0.007		0.770
IgG (mg/dL)[a]		(n=1,762)		
	--	r = 0.034		0.150
IgM (mg/dL)[a]		(n=1,762)		
	--	r = -0.001		0.970
Lupus Panel: ANA Test		(n=1,144)	(n=618)	
	Present	20.0%	17.5%	0.218
Lupus Panel: Thyroid Microsomal Antibody		(n=1,144)	(n=618)	
	Present	2.5%	3.1%	0.532
Lupus Panel: MSK Anti-smooth Muscle Antibody		(n=1,144)	(n=618)	
	Present	0.7%	1.5%	0.195
Lupus Panel: MSK Anti-mitochondrial Antibody		(n=1,144)	(n=618)	
	Present	0.3%	0.2%	0.999
Lupus Panel: MSK Anti-parietal Cell Antibody		(n=1,144)	(n=618)	
	Present	2.3%	3.7%	0.107
Lupus Panel: Rheumatoid Factor		(n=1,144)	(n=618)	
	Present	20.0%	24.8%	0.025

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				p-Value
		Never	Former	>0-20	>20	
CD3+ Cells (T Cells) (cells/mm^3)[a]			(n=692)			
	--		r = 0.197			<0.001
CD4+ Cells (Helper T Cells) (cells/mm^3)[b]			(n=692)			
	--		r = 0.215			<0.001
CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]			(n=692)			
	--		r = 0.079			0.038

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				
		Never	Former	>0-20	>20	p-Value
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]			(n=692)			
	--		r = -0.077			0.042
CD20+ Cells (B Cells) (cells/mm^3)[a]			(n=692)			
	--		r = 0.132			0.001
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[b]			(n=692)			
	--		r = 0.228			<0.001
Absolute Lymphocytes (cells/mm^3)[a]			(n=1,761)			
	--		r = 0.151			<0.001
IgA (mg/dL)[b]			(n=1,761)			
	--		r = -0.045			0.061
IgG (mg/dL)[a]			(n=1,761)			
	--		r = -0.073			0.002
IgM (mg/dL)[a]			(n=1,761)			
	--		r = 0.008			0.750
Lupus Panel: ANA Test		(n=544)	(n=966)	(n=197)	(n=54)	
	Present	20.0%	18.6%	17.3%	26.0%	0.475
Lupus Panel: Thyroid Microsomal Antibody		(n=544)	(n=966)	(n=197)	(n=54)	
	Present	2.4%	2.8%	2.5%	3.7%	0.928
Lupus Panel: MSK Anti-smooth Muscle Antibody		(n=544)	(n=966)	(n=197)	(n=54)	
	Present	0.9%	0.9%	1.5%	0.0%	0.755
Lupus Panel: MSK Anti-mitochondrial Antibody		(n=544)	(n=966)	(n=197)	(n=54)	
	Present	0.4%	0.1%	0.5%	0.0%	0.587
Lupus Panel: MSK Anti-parietal Cell Antibody		(n=544)	(n=966)	(n=197)	(n=54)	
	Present	2.8%	3.0%	2.0%	1.9%	0.859
Lupus Panel: Rheumatoid Factor		(n=544)	(n=966)	(n=197)	(n=54)	
	Present	17.7%	21.6%	31.0%	29.6%	<0.001

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	>0-10	>10	p-Value
CD3+ Cells (T Cells) (cells/mm^3)[a]			(n=691)		
	--		r = 0.088		0.021
CD4+ Cells (Helper T Cells) (cells/mm^3)[b]			(n=691)		
	--		r = 0.076		0.047
CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]			(n=691)		
	--		r = 0.081		0.033
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]			(n=691)		
	--		r = 0.022		0.563
CD20+ Cells (B Cells) (cells/mm^3)[a]			(n=691)		
	--		r = -0.034		0.369
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[b]			(n=691)		
	--		r = 0.076		0.046

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	**>0-10**	**>10**	**p-Value**
Absolute Lymphocytes (cells/mm^3)[a]			(n=1,760)		
	--		r = 0.067		0.005
IgA (mg/dL)[b]			(n=1,760)		
	--		r = 0.007		0.776
IgG (mg/dL)[a]			(n=1,760)		
	--		r = -0.036		0.133
IgM (mg/dL)[a]			(n=1,760)		
	--		r = 0.011		0.656
Lupus Panel: ANA Test		(n=544)	(n=449)	(n=767)	
	Present	20.0%	14.9%	21.0%	0.028
Lupus Panel: Thyroid Microsomal Antibody		(n=544)	(n=449)	(n=767)	
	Present	2.4%	3.1%	2.6%	0.770
Lupus Panel: MSK Anti-smooth Muscle Antibody		(n=544)	(n=449)	(n=767)	
	Present	0.9%	1.3%	0.8%	0.629
Lupus Panel: MSK Anti-mitochondrial Antibody		(n=544)	(n=449)	(n=767)	
	Present	0.4%	0.0%	0.3%	0.465
Lupus Panel: MSK Anti-parietal Cell Antibody		(n=544)	(n=449)	(n=767)	
	Present	2.8%	3.6%	2.4%	0.461
Lupus Panel: Rheumatoid Factor		(n=544)	(n=449)	(n=767)	
	Present	17.7%	19.8%	25.7%	0.001

Dependent Variable	Level	Current Alcohol Use (drinks/day)		
		0-1	**>1**	**p-Value**
CD3+ Cells (T Cells) (cells/mm^3)[a]		(n=692)		
	--	r = -0.069		0.070
CD4+ Cells (Helper T Cells) (cells/mm^3)[b]		(n=692)		
	--	r = -0.057		0.134
CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]		(n=692)		
	--	r = -0.059		0.123
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]		(n=692)		
	--	r = 0.028		0.468
CD20+ Cells (B Cells) (cells/mm^3)[a]		(n=692)		
	--	r = -0.114		0.003
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[b]		(n=692)		
	--	r = -0.059		0.124
Absolute Lymphocytes (cells/mm^3)[a]		(n=1,761)		
	--	r = -0.043		0.071
IgA (mg/dL)[b]		(n=1,761)		
	--	r = 0.029		0.223
IgG (mg/dL)[a]		(n=1,761)		
	--	r = -0.069		0.004

Dependent Variable	Level	Current Alcohol Use (drinks/day)		p-Value
		0-1	>1	
IgM (mg/dL)[a]		(n=1,761)		
	--	r = 0.023		0.337
Lupus Panel: ANA Test		(n=1,502)	(n=259)	
	Present	18.7%	21.6%	0.310
Lupus Panel: Thyroid Microsomal Antibody		(n=1,502)	(n=259)	
	Present	2.9%	1.2%	0.154
Lupus Panel: MSK Anti-smooth Muscle Antibody		(n=1,502)	(n=259)	
	Present	1.0%	0.8%	0.999
Lupus Panel: MSK Anti-mitochondrial Antibody		(n=1,502)	(n=259)	
	Present	0.3%	0.0%	0.901
Lupus Panel: MSK Anti-parietal Cell Antibody		(n=1,502)	(n=259)	
	Present	3.0%	1.5%	0.268
Lupus Panel: Rheumatoid Factor		(n=1,502)	(n=259)	
	Present	20.8%	27.0%	0.030

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			p-Value
		0	>0-40	>40	
CD3+ Cells (T Cells) (cells/mm^3)[a]			(n=691)		
	--		r = -0.006		0.868
CD4+ Cells (Helper T Cells) (cells/mm^3)[b]			(n=691)		
	--		r = 0.006		0.883
CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]			(n=691)		
	--		r = -0.031		0.421
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]			(n=691)		
	--		r = 0.001		0.983
CD20+ Cells (B Cells) (cells/mm^3)[a]			(n=691)		
	--		r = -0.079		0.039
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[b]			(n=691)		
	--		r = 0.010		0.799
Absolute Lymphocytes (cells/mm^3)[a]			(n=1,758)		
	--		r = 0.022		0.362
IgA (mg/dL)[b]			(n=1,758)		
	--		r = 0.056		0.018
IgG (mg/dL)[a]			(n=1,758)		
	--		r = -0.046		0.056
IgM (mg/dL)[a]			(n=1,758)		
	--		r = 0.019		0.438
Lupus Panel: ANA Test		(n=98)	(n=1,120)	(n=540)	
	Present	14.3%	19.4%	19.6%	0.447
Lupus Panel: Thyroid Microsomal Antibody		(n=98)	(n=1,120)	(n=540)	
	Present	2.0%	3.0%	2.2%	0.640

Dependent Variable	Level	Lifetime Alcohol History (drink-years)			
		0	>0-40	>40	p-Value
Lupus Panel: MSK Anti-smooth Muscle Antibody		(n=98)	(n=1,120)	(n=540)	
	Present	0.0%	1.3%	0.6%	0.241
Lupus Panel: MSK Anti-mitochondrial Antibody		(n=98)	(n=1,120)	(n=540)	
	Present	0.0%	0.3%	0.2%	0.841
Lupus Panel: MSK Anti-parietal Cell Antibody		(n=98)	(n=1,120)	(n=540)	
	Present	4.1%	3.1%	1.9%	0.244
Lupus Panel: Rheumatoid Factor		(n=98)	(n=1,120)	(n=540)	
	Present	21.4%	20.3%	24.8%	0.109

Dependent Variable	Level	Physical Activity Index (kcal/kg/day)			
		Sedentary (<1.45)	Moderate (1.45-<2.95)	Very Active (≥2.95)	p-Value
CD3+ Cells (T Cells) (cells/mm^3)[a]		(n=357)	(n=138)	(n=197)	
	--	O = 1,262.3	O = 1,154.2	O = 1,172.2	0.026
CD4+ Cells (Helper T Cells) (cells/mm^3)[b]		(n=357)	(n=138)	(n=197)	
	--	O = 900.0	O = 833.1	O = 867.5	0.126
CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]		(n=357)	(n=138)	(n=197)	
	--	O = 543.6	O = 493.6	O = 500.3	0.053
CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]		(n=357)	(n=138)	(n=197)	
	--	O = 230.1	O = 220.9	O = 212.3	0.222
CD20+ Cells (B Cells) (cells/mm^3)[a]		(n=357)	(n=138)	(n=197)	
	--	O = 196.0	O = 171.9	O = 178.5	0.076
CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[b]		(n=357)	(n=138)	(n=197)	
	--	O = 831.8	O = 767.5	O = 799.2	0.121
Absolute Lymphocytes (cells/mm^3)[a]		(n=880)	(n=351)	(n=530)	
	--	O = 1,717.7	O = 1,565.2	O = 1,621.6	<0.001
IgA (mg/dL)[b]		(n=880)	(n=351)	(n=530)	
	--	O = 262.8	O = 242.0	O = 257.0	0.024
IgG (mg/dL)[a]		(n=880)	(n=351)	(n=530)	
	--	O = 1,061.1	O = 1,045.8	O = 1,062.0	0.621
IgM (mg/dL)[a]		(n=880)	(n=351)	(n=530)	
	--	O = 90.26	O = 88.03	O = 92.74	0.453
Lupus Panel: ANA Test		(n=880)	(n=351)	(n=530)	
	Present	18.8%	19.1%	19.8%	0.886
Lupus Panel: Thyroid Microsomal Antibody		(n=880)	(n=351)	(n=530)	
	Present	3.6%	2.0%	1.5%	0.038
Lupus Panel: MSK Anti-smooth Muscle Antibody		(n=880)	(n=351)	(n=530)	
	Present	1.4%	0.3%	0.8%	0.182

Dependent Variable	Level	Physical Activity Index (kcal/kg/day)			p-Value
		Sedentary (<1.45)	Moderate (1.45-<2.95)	Very Active (≥2.95)	
Lupus Panel: MSK Anti-mitochondrial Antibody		(n=880)	(n=351)	(n=530)	
	Present	0.1%	0.0%	0.6%	0.136
Lupus Panel: MSK Anti-parietal Cell Antibody		(n=880)	(n=351)	(n=530)	
	Present	2.8%	2.3%	3.0%	0.799
Lupus Panel: Rheumatoid Factor		(n=880)	(n=351)	(n=530)	
	Present	21.9%	22.5%	20.8%	0.802

[a]Analysis performed on natural logarithm scale; means transformed from natural logarithm scale.

[b]Analysis performed on square root scale; means transformed from square root scale.

Note: Correlations (r) are based on total sample size and are not category-specific.

Please see Section 19.1.3 and Table 19-2 for a further discussion of the dependent variables and covariates shown in this appendix.

Table F-12. Dependent Variable-covariate Associations for the Pulmonary Assessment

Dependent Variable	Level	Age			Race		
		Born ≥1942	Born <1942	p-Value	Black	Non-Black	p-Value
Asthma		(n=886)	(n=1,050)		(n=124)	(n=1,812)	
	Yes	4.9%	7.8%	0.011	4.0%	6.6%	0.344
Bronchitis		(n=879)	(n=1,028)		(n=123)	(n=1,784)	
	Yes	28.6%	33.4%	0.027	23.6%	31.7%	0.076
Pneumonia		(n=875)	(n=995)		(n=122)	(n=1,748)	
	Yes	11.4%	15.9%	0.007	13.9%	13.8%	0.999
Thorax and Lung Abnormality		(n=890)	(n=1,060)		(n=125)	(n=1,825)	
	Yes	15.7%	20.4%	0.010	14.4%	18.5%	0.301
X-ray Interpretation		(n=888)	(n=1,060)		(n=125)	(n=1,823)	
	Abnormal	13.1%	19.6%	<0.001	16.0%	16.7%	0.943
FVC (% of predicted)		(n=882)	(n=1,047)		(n=125)	(n=1,804)	
(continuous)	--	r = 0.010		0.655	O = 87.88	O = 102.26	<0.001
(discrete)	Low	9.0%	10.3%	0.354	27.2%	8.5%	<0.001
FEV_1 (% of predicted)		(n=882)	(n=1,047)		(n=125)	(n=1,804)	
(continuous)	--	r = -0.113		<0.001	O = 81.50	O = 89.43	<0.001
(discrete)	Low	25.5%	34.1%	<0.001	42.4%	29.3%	0.003
Ratio of Observed FEV_1 to Observed FVC^a		(n=1,929)			(n=125)	(n=1,804)	
	--	r = 0.271		<0.001	O = 0.752	O = 0.713	<0.001
Loss of Vital Capacity		(n=879)	(n=1,044)		(n=122)	(n=1,801)	
	None	92.4%	91.8%	0.039	75.4%	93.2%	<0.001
	Mild	6.5%	5.6%		18.9%	5.1%	
	Moderate or Severe	1.1%	2.7%		5.7%	1.7%	
Obstructive Abnormality		(n=879)	(n=1,043)		(n=121)	(n=1,801)	
	None	64.6%	44.3%	<0.001	62.0%	53.0%	0.042
	Mild	28.4%	42.0%		26.5%	36.4%	
	Moderate	6.0%	9.2%		10.7%	7.6%	
	Severe	0.9%	4.5%		0.8%	3.0%	

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
Asthma		(n=764)	(n=316)	(n=856)	
	Yes	6.5%	6.3%	6.4%	0.990
Bronchitis		(n=748)	(n=308)	(n=851)	
	Yes	30.5%	32.1%	31.4%	0.853
Pneumonia		(n=731)	(n=298)	(n=841)	
	Yes	14.5%	14.8%	12.8%	0.553
Thorax and Lung Abnormality		(n=768)	(n=318)	(n=864)	
	Yes	12.0%	27.0%	20.6%	<0.001

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Table F-12. Dependent Variable-covariate Associations for the Pulmonary Assessment (Continued)

Dependent Variable	Level	Military Occupation			
		Officer	Enlisted Flyer	Enlisted Groundcrew	p-Value
X-ray Interpretation		(n=767)	(n=318)	(n=863)	
	Low	16.2%	18.9%	16.2%	0.504
FVC (% of predicted)		(n=763)	(n=313)	(n=853)	
(continuous)	--	Ō = 103.50	Ō = 100.17	Ō = 99.81	<0.001
(discrete)	Low	7.2%	12.1%	11.0%	0.010
FEV$_1$ (% of predicted)		(n=763)	(n=313)	(n=853)	
(continuous)	--	Ō = 90.61	Ō = 85.59	Ō = 88.61	<0.001
(discrete)	Low	27.4%	39.6%	29.2%	<0.001
Ratio of Observed FEV$_1$ to Observed FVC		(n=763)	(n=313)	(n=853)	
	--	Ō = 0.708	Ō = 0.698	Ō = 0.728	<0.001
Loss of Vital Capacity		(n=763)	(n=311)	(n=849)	
	None	94.4%	89.7%	90.8%	0.020
	Mild	3.8%	8.4%	7.1%	
	Moderate or Severe	1.8%	1.9%	2.1%	
Obstructive Abnormality		(n=763)	(n=310)	(n=849)	
	None	49.0%	44.2%	61.1%	<0.001
	Mild	42.1%	39.4%	28.9%	
	Moderate	6.2%	12.3%	7.5%	
	Severe	2.8%	4.2%	2.5%	

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				
		Never	Former	>0–20	>20	p-Value
Thorax and Lung Abnormality		(n=601)	(n=1,075)	(n=214)	(n=58)	
	Yes	5.2%	15.1%	55.6%	74.1%	<0.001
X-ray Interpretation		(n=600)	(n=1,074)	(n=214)	(n=58)	
	Abnormal	15.3%	15.6%	23.4%	24.1%	0.013
FVC (% of predicted)		(n=596)	(n=1,061)	(n=213)	(n=58)	
(continuous)	--	r =-0.040				0.077
(discrete)	Low	7.2%	10.3%	13.6%	8.6%	0.038
FEV$_1$ (% of predicted)		(n=596)	(n=1,061)	(n=213)	(n=58)	
(continuous)	--	r = -0.201				<0.001
(discrete)	Low	18.3%	31.8%	46.0%	63.8%	<0.001
Ratio of Observed FEV$_1$ to Observed FVC[a]		(n=1,928)				
	--	r =0.219				<0.001
Loss of Vital Capacity		(n=595)	(n=1,060)	(n=209)	(n=58)	
	None	94.5%	91.2%	88.5%	96.6%	0.045
	Mild	3.9%	6.5%	9.6%	3.5%	
	Moderate or Severe	1.7%	2.3%	1.9%	0.0%	

Dependent Variable	Level	Current Cigarette Smoking (cigarettes/day)				
		Never	Former	>0–20	>20	p-Value
Obstructive Abnormality		(n=595)	(n=1,059)	(n=209)	(n=58)	
	None	66.2%	52.1%	34.9%	19.0%	<0.001
	Mild	29.1%	37.1%	45.5%	46.6%	
	Moderate	4.0%	7.4%	14.8%	25.9%	
	Severe	0.7%	3.4%	4.8%	8.6%	

Dependent Variable	Level	Lifetime Cigarette Smoking History (pack-years)			
		0	>0–10	>10	p-Value
Asthma		(n=598)	(n=486)	(n=849)	
	Yes	6.4%	6.0%	6.8%	0.819
Bronchitis		(n=591)	(n=479)	(n=834)	
	Yes	26.9%	29.2%	35.4%	0.002
Pneumonia		(n=581)	(n=474)	(n=812)	
	Yes	12.1%	12.5%	15.9%	0.075
Thorax and Lung Abnormality		(n=601)	(n=491)	(n=855)	
	Yes	5.2%	15.1%	29.2%	<0.001
X-ray Interpretation		(n=600)	(n=490)	(n=855)	
	Abnormal	15.3%	14.1%	19.1%	0.036
FVC (% of predicted)		(n=596)	(n=483)	(n=848)	
(continuous)	--		r = -0.118		<0.001
(discrete)	Low	7.2%	8.1%	12.3%	0.002
FEV$_1$ (% of predicted)		(n=596)	(n=483)	(n=848)	
(continuous)	--		r = -0.294		<0.001
(discrete)	Low	18.3%	23.2%	42.5%	<0.001
Ratio of Observed FEV$_1$ to Observed FVC[a]	--		(n=1,927) r = 0.283		<0.001
Loss of Vital Capacity		(n=595)	(n=483)	(n=843)	
	None	94.5%	93.0%	89.9%	0.019
	Mild	3.9%	5.8%	7.5%	
	Moderate or Severe	1.7%	1.2%	2.6%	
Obstructive Abnormality		(n=595)	(n=483)	(n=842)	
	None	66.2%	60.3%	40.9%	<0.001
	Mild	29.1%	31.1%	43.4%	
	Moderate	4.0%	6.8%	10.8%	
	Severe	0.7%	1.9%	5.0%	

Dependent Variable	Level	Body Mass Index			Lifetime Exposure to Industrial Chemicals		
		Not Obese ($\leq$30)	Obese (>30)	p-Value	Yes	No	p-Value
Asthma		(n=1,250)	(n=685)		(n=1,204)	(n=732)	
	Yes	6.7%	6.0%	0.595	6.6%	6.3%	0.884
Bronchitis		(n=1,230)	(n=676)		(n=1,188)	(n=719)	
	Yes	29.6%	33.9%	0.060	32.2%	29.5%	0.242
Pneumonia		(n=1,209)	(n=660)		(n=1,170)	(n=700)	
	Yes	13.6%	14.2%	0.737	13.5%	14.3%	0.686
Thorax and Lung Abnormality	Yes	(n=1,261) 19.3%	(n=689) 16.4%	0.132	(n=1,217) 20.3%	(n=733) 14.9%	0.003
X-ray Interpretation	Abnormal	(n=1,259) 16.5%	(n=689) 16.8%	0.909	(n=1,216) 16.3%	(n=732) 17.2%	0.638
FVC (% of predicted)		(n=1,249)	(n=680)		(n=1,203)	(n=726)	
(continuous)	--	r = -0.286		<0.001	O = 100.76	O = 102.26	0.054
(discrete)	Low	7.3%	14.1%	<0.001	10.9%	7.7%	0.028
FEV_1 (% of predicted)		(n=1,249)	(n=680)		(n=1,203)	(n=726)	
(continuous)	--	r = -0.099		<0.001	O = 88.48	O = 89.63	0.160
(discrete)	Low	28.4%	33.4%	0.027	30.8%	29.1%	0.440
Ratio of Observed FEV_1 to Observed FVC[a]		(n=1,929)			(n=1,203)	(n=726)	
	--	r = -0.206		<0.001	O = 0.718	O = 0.711	0.092
Loss of Vital Capacity		(n=1,244)	(n=679)		(n=1,198)	(n=725)	
	None	94.2%	88.1%	<0.001	91.2%	93.5%	0.177
	Mild	4.4%	8.8%		6.7%	4.8%	
	Moderate or Severe	1.4%	3.1%		2.2%	1.7%	
Obstructive Abnormality		(n=1,243)	(n=679)		(n=1,198)	(n=724)	
	None	50.3%	59.7%	<0.001	54.9%	51.4%	0.235
	Mild	39.3%	29.3%		34.1%	38.7%	
	Moderate	7.3%	8.5%		8.0%	7.3%	
	Severe	3.1%	2.5%		3.0%	2.6%	

[a]Analysis performed on natural logarithm of (1 − ratio of observed FEV_1 to observed FVC) scale; means transformed from natural logarithm of (1 − ratio of observed FEV_1 to observed FVC) scale. Because of this transformation, a positive (or negative) correlation implies a negative (or positive) association between the ratio and the covariate.

Note: Correlations (r) are based on total sample size and are not category-specific.

Please see Section 20.1.3 and Table 20-1 for a further discussion of the dependent variables and covariates shown in this appendix.

APPENDIX G

List of Tables

APPENDIX G. SUMMARY OF ANALYSIS RESULTS

This appendix contains a summary of the results from the exposure analyses performed for this report and contained in Chapters 9 through 20. This summary is organized into 24 tables, grouped by analysis (unadjusted or adjusted), data form (continuous, dichotomous, or polytomous), and model (1, 2, 3, or 4). Each table contains a reference to its corresponding table in Chapters 9 through 20 and a description of the clinical parameter being summarized. The summary statistics, grouped by model and presented for each analysis and data form, are described below.

G.1 Model 1

For analyses of continuous data using Model 1 (Tables G-1 and G-13), the occupational category, Ranch Hand mean, Comparison mean, difference of Ranch Hand and Comparison means along with the associated 95-percent confidence interval (referred to as "C.I." throughout the following tables), and p-value are given for the unadjusted and adjusted analyses. For analyses of dichotomous data using Model 1 (Tables G-5 and G-17), the occupational category, unadjusted or adjusted relative risk and associated 95-percent C.I., and p-value are given for the unadjusted and adjusted analyses. The number and percentage of abnormalities within the Ranch Hand and Comparison groups are given for the unadjusted analyses. For analyses of polytomous data using Model 1 (Tables G-9 and G-21), the contrast (of the specified abnormal category versus the normal category), occupational category, unadjusted or adjusted relative risk and associated 95-percent C.I., and p-value are given for the unadjusted and adjusted analyses. The number and percentage of Ranch Hands and Comparisons within each abnormal level are given for the unadjusted analyses.

G.2 Models 2 and 4

For analyses of continuous data using Models 2 and 4 (Tables G-2 and G-14 for Model 2, Tables G-4 and G-16 for Model 4), the coefficient of determination (R^2), slope, standard error, and p-value are given for the unadjusted and adjusted analyses. For analyses of dichotomous data using Models 2 and 4 (Tables G-6 and G-18 for Model 2, Tables G-8 and G-20 for Model 4), the unadjusted or adjusted relative risk and associated 95-percent C.I., and p-value are given for the unadjusted and adjusted analyses. For analyses of polytomous data using Models 2 and 4 (Tables G-10 and G-22 for Model 2, Tables G-12 and G-24 for Model 4), the contrast (of the specified abnormal category versus the normal category), the unadjusted or adjusted relative risk and associated 95-percent C.I., and p-value are given for the unadjusted and adjusted analyses.

G.3 Model 3

For analyses of continuous data using Model 3 (Tables G-3 and G-17), the R^2, dioxin category, dioxin category sample size (n) and mean, difference of Ranch Hand dioxin category and Comparison dioxin category means along with the associated 95-percent C.I., and p-value are given for the unadjusted and adjusted analyses. For analyses of dichotomous data using Model 3 (Tables G-7 and G-19), the dioxin category, sample size, unadjusted or adjusted relative risk and associated 95-percent C.I. for each Ranch Hand category versus Comparison contrast, and p-value are given for the unadjusted and adjusted analyses. The number and percentage of abnormalities within each dioxin category are given for unadjusted analyses. For analyses of polytomous data using Model 3 (Tables G-11 and G-23), the

contrast (of the specified abnormal category versus the normal category), dioxin category, sample size, unadjusted or adjusted relative risk and associated 95-percent C.I. for each Ranch Hand category versus Comparison contrast, and p-value are given for the unadjusted and adjusted analyses. The number and percentage of each abnormal level within each dioxin category are given for the unadjusted analyses.

A summary of the analysis (unadjusted or adjusted), data form (continuous, dichotomous, or polytomous), and model (1, 2, 3, or 4) for each table in Appendix G is given below.

Appendix G Table	Analysis	Data Form	Model
G-1	Unadjusted	Continuous	1
G-2	Unadjusted	Continuous	2
G-3	Unadjusted	Continuous	3
G-4	Unadjusted	Continuous	4
G-5	Unadjusted	Dichotomous	1
G-6	Unadjusted	Dichotomous	2
G-7	Unadjusted	Dichotomous	3
G-8	Unadjusted	Dichotomous	4
G-9	Unadjusted	Polytomous	1
G-10	Unadjusted	Polytomous	2
G-11	Unadjusted	Polytomous	3
G-12	Unadjusted	Polytomous	4
G-13	Adjusted	Continuous	1
G-14	Adjusted	Continuous	2
G-15	Adjusted	Continuous	3
G-16	Adjusted	Continuous	4
G-17	Adjusted	Dichotomous	1
G-18	Adjusted	Dichotomous	2
G-19	Adjusted	Dichotomous	3
G-20	Adjusted	Dichotomous	4
G-21	Adjusted	Polytomous	1
G-22	Adjusted	Polytomous	2
G-23	Adjusted	Polytomous	3
G-24	Adjusted	Polytomous	4

Table G-1. Summary of Unadjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Mean Ranch Hand	Mean Comparison	Difference of Means (95% C.I.)	p-Value
9-6	Body Mass Index $(kg/m^2)^a$	All	28.67	28.70	-0.03	0.880
		Officer	28.34	28.29	-0.06	0.846
		Enlisted Flyer	28.48	28.90	-0.42	0.382
		Enlisted Groundcrew	29.04	28.99	0.05	0.873
10-37	PSA $(ng/mL)^a$	All	0.95	0.97	-0.02	0.644
		Officer	0.98	1.10	-0.12	0.078
		Enlisted Flyer	1.12	1.02	0.10	0.318
		Enlisted Groundcrew	0.87	0.86	0.01	0.778
12-20	WMS-R: Verbal Paired Associates	All	11.02	10.96	0.06 (-0.23,0.35)	0.674
		Officer	11.65	11.54	0.12 (-0.34,0.57)	0.615
		Enlisted Flyer	10.00	10.23	-0.23 (-0.94,0.47)	0.520
		Enlisted Groundcrew	10.85	10.71	0.14 (-0.29,0.58)	0.526
12-21	WMS-R: Logical Memory, Immediate Recall	All	11.70	11.58	0.12 (-0.18,0.42)	0.431
		Officer	12.59	12.60	-0.01 (-0.48,0.45)	0.957
		Enlisted Flyer	10.66	10.92	-0.26 (-0.97,0.46)	0.483
		Enlisted Groundcrew	11.30	10.91	0.38 (-0.06,0.83)	0.089
12-22	WMS-R: Logical Memory, Delayed Recall	All	9.59	9.40	0.19 (-0.14,0.53)	0.250
		Officer	10.58	10.65	-0.08 (-0.59,0.43)	0.770
		Enlisted Flyer	8.41	8.57	-0.16 (-0.94,0.63)	0.696
		Enlisted Groundcrew	9.16	8.59	0.57 (0.08,1.05)	0.021
12-23	WMS-R: Visual Reproduction, Immediate Recall	All	27.94	27.84	0.10 (-0.34,0.54)	0.663
		Officer	28.79	28.78	0.01 (-0.68,0.70)	0.973
		Enlisted Flyer	25.99	26.45	-0.46 (-1.52,0.60)	0.395
		Enlisted Groundcrew	27.93	27.50	0.43 (-0.22,1.08)	0.197
12-24	WMS-R: Visual Reproduction, Delayed Recall	All	26.34	26.09	0.24 (-0.34,0.83)	0.409
		Officer	27.47	27.38	0.10 (-0.81,1.01)	0.834
		Enlisted Flyer	24.05	24.47	-0.42 (-1.82,0.99)	0.560
		Enlisted Groundcrew	26.20	25.53	0.67 (-0.19,1.54)	0.127
13-11	AST $(U/L)^a$	All	24.49	24.17	0.32	0.363
		Officer	25.37	24.34	1.03	0.075
		Enlisted Flyer	23.15	23.85	-0.70	0.406
		Enlisted Groundcrew	24.26	24.13	0.13	0.812
13-13	ALT $(U/L)^a$	All	44.76	44.60	0.16	0.772
		Officer	44.83	43.65	1.18	0.180
		Enlisted Flyer	43.00	43.66	-0.66	0.620
		Enlisted Groundcrew	45.42	45.80	-0.38	0.663
13-15	GGT $(U/L)^a$	All	45.32	45.41	-0.10	0.929
		Officer	43.72	43.16	0.56	0.741
		Enlisted Flyer	43.74	45.87	-2.14	0.425
		Enlisted Groundcrew	47.52	47.36	0.16	0.926

Table Ref.	Clinical Parameter (Units)	Occupational Category	Mean		Difference of Means (95% C.I.)	p-Value
			Ranch Hand	Comparison		
13-17	Alkaline Phosphatase (U/L)[a]	All	94.58	92.32	2.26	0.048
		Officer	89.72	88.66	1.06	0.537
		Enlisted Flyer	96.82	94.54	2.28	0.423
		Enlisted Groundcrew	98.37	94.92	3.46	0.052
13-19	Total Bilirubin (mg/dL)[a]	All	0.518	0.518	0.001	0.964
		Officer	0.552	0.557	-0.006	0.779
		Enlisted Flyer	0.499	0.489	0.010	0.710
		Enlisted Groundcrew	0.496	0.494	0.002	0.908
13-22	LDH (U/L)[a]	All	154.1	151.9	2.2	0.089
		Officer	155.8	151.7	4.1	0.049
		Enlisted Flyer	152.1	151.7	0.4	0.892
		Enlisted Groundcrew	153.4	152.1	1.2	0.531
13-24	Cholesterol (mg/dL)[b]	All	194.8	197.6	-2.8	0.102
		Officer	190.7	194.7	-4.0	0.132
		Enlisted Flyer	196.4	198.6	-2.2	0.604
		Enlisted Groundcrew	198.0	199.8	-1.8	0.481
13-26	HDL Cholesterol (mg/dL)[a]	All	44.35	44.60	-0.25	0.643
		Officer	47.22	47.01	0.21	0.814
		Enlisted Flyer	43.51	43.21	0.30	0.818
		Enlisted Groundcrew	42.18	43.04	-0.86	0.270
13-28	Cholesterol-HDL Ratio[a]	All	4.36	4.39	-0.04	0.543
		Officer	4.01	4.11	-0.10	0.228
		Enlisted Flyer	4.48	4.56	-0.08	0.574
		Enlisted Groundcrew	4.65	4.60	0.05	0.556
13-30	Triglycerides (mg/dL)[a]	All	134.8	133.5	1.3	0.695
		Officer	122.8	122.1	0.7	0.876
		Enlisted Flyer	140.1	142.8	-2.7	0.746
		Enlisted Groundcrew	144.5	141.1	3.4	0.516
13-32	Creatine Phosphokinase (U/L)[a]	All	107.6	106.3	1.3	0.672
		Officer	104.0	102.4	1.6	0.725
		Enlisted Flyer	97.0	104.3	-7.4	0.286
		Enlisted Groundcrew	115.7	110.7	5.1	0.290
13-34	Serum Amylase (U/L)[a]	All	54.37	55.48	-1.11	0.263
		Officer	52.92	55.90	-2.99	0.056
		Enlisted Flyer	54.07	55.76	-1.69	0.489
		Enlisted Groundcrew	55.86	55.00	0.86	0.571
13-40	Prealbumin (mg/dL)[b]	All	28.99	28.80	0.19	0.488
		Officer	29.05	28.92	0.12	0.771
		Enlisted Flyer	28.94	28.30	0.64	0.326
		Enlisted Groundcrew	28.95	28.87	0.08	0.844
13-42	Albumin (mg/dl)	All	4,187.9	4,187.0	0.9 (-24.3,26.1)	0.945
		Officer	4,161.3	4,174.5	-13.2 (-53.1,26.7)	0.517
		Enlisted Flyer	4,210.5	4,195.6	14.9 (-46.7,76.6)	0.635
		Enlisted Groundcrew	4,203.3	4,195.1	8.2 (-29.9,46.3)	0.673

Table G-1. Summary of Unadjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Mean Ranch Hand	Mean Comparison	Difference of Means (95% C.I.)	p-Value
13-44	α-1-Acid Glycoprotein (mg/dl)[a]	All	78.51	78.09	0.42	0.632
		Officer	74.83	75.96	-1.14	0.395
		Enlisted Flyer	80.37	79.45	0.92	0.673
		Enlisted Groundcrew	81.31	79.56	1.75	0.198
13-46	α-1-Antitrypsin (mg/dL)[b]	All	142.1	140.2	1.9	0.119
		Officer	137.2	136.6	0.6	0.753
		Enlisted Flyer	147.0	146.7	0.4	0.902
		Enlisted Groundcrew	144.7	141.1	3.5	0.056
13-48	α-2-Macroglobulin (mg/dL)[a]	All	185.7	186.1	-0.3	0.898
		Officer	187.2	184.1	3.1	0.458
		Enlisted Flyer	194.5	199.9	-5.5	0.426
		Enlisted Groundcrew	181.0	183.1	-2.2	0.582
13-50	Apolipoprotein B (mg/dL)[b]	All	102.1	103.1	-1.0	0.372
		Officer	98.0	99.8	-1.7	0.314
		Enlisted Flyer	104.6	104.8	-0.2	0.955
		Enlisted Groundcrew	104.9	105.5	-0.6	0.721
13-52	C3 Complement (mg/dL)[b]	All	119.9	119.2	0.7	0.461
		Officer	114.2	112.8	1.4	0.355
		Enlisted Flyer	121.8	122.8	-1.1	0.651
		Enlisted Groundcrew	124.6	123.7	0.9	0.565
13-54	C4 Complement (mg/dL)[b]	All	22.41	22.74	-0.33	0.209
		Officer	21.44	22.27	-0.83	0.044
		Enlisted Flyer	22.95	22.42	0.53	0.413
		Enlisted Groundcrew	23.11	23.29	-0.18	0.657
13-56	Haptoglobin (mg/dL)[b]	All	126.9	119.0	7.9	0.005
		Officer	114.5	108.9	5.6	0.184
		Enlisted Flyer	136.1	132.0	4.2	0.559
		Enlisted Groundcrew	135.1	123.9	11.2	0.010
13-58	Transferrin (mg/dL)[a]	All	255.4	253.9	1.5	0.441
		Officer	249.7	250.9	-1.2	0.684
		Enlisted Flyer	257.7	254.7	3.1	0.510
		Enlisted Groundcrew	259.8	256.4	3.4	0.242
13-60	Prothrombin Time (seconds)[a]	All	10.74	10.71	0.04	0.183
		Officer	10.78	10.74	0.04	0.338
		Enlisted Flyer	10.74	10.72	0.02	0.758
		Enlisted Groundcrew	10.71	10.67	0.04	0.373
14-11	Duration of Post SEA Acne (months) (Excluding Participants with Pre-SEA Acne)[b]	All	67.88	52.66	15.23	0.172
		Officer	48.11	32.66	15.45	0.406
		Enlisted Flyer	53.03	93.28	-40.25	0.197
		Enlisted Groundcrew	79.16	54.56	24.60	0.096

Table Ref.	Clinical Parameter (Units)	Occupational Category	Mean Ranch Hand	Comparison	Difference of Means (95% C.I.)	p-Value
14-12	Duration of Post-SEA Acne (months) (All Post-SEA Occurrences)[b]	All	126.10	134.59	-8.49	0.549
		Officer	121.23	139.63	-18.40	0.492
		Enlisted Flyer	113.86	161.89	-48.03	0.197
		Enlisted Groundcrew	131.99	125.21	6.78	0.718
15-7	Systolic Blood Pressure (mm Hg)[a]	All	127.8	129.3	-1.5	0.064
		Officer	129.1	129.6	-0.5	0.687
		Enlisted Flyer	129.2	130.7	-1.5	0.450
		Enlisted Groundcrew	126.1	128.5	-2.4	0.045
15-9	Diastolic Blood Pressure (mm Hg)[b]	All	74.73	75.02	-0.29	0.517
		Officer	73.52	73.60	-0.08	0.905
		Enlisted Flyer	74.65	74.83	-0.18	0.869
		Enlisted Groundcrew	75.85	76.33	-0.48	0.481
15-29	Resting Pressure Index	All	1.250	1.253	-0.004 (-0.017,0.010)	0.591
		Officer	1.266	1.270	-0.005 (-0.026,0.017)	0.670
		Enlisted Flyer	1.226	1.234	-0.008 (-0.040,0.025)	0.652
		Enlisted Groundcrew	1.245	1.246	-0.001 (-0.021,0.019)	0.920
15-31	Hyperemic Pressure Index (1 Minute Post-exercise)	All	1.175	1.172	0.003 (-0.014,0.021)	0.697
		Officer	1.204	1.202	0.001 (-0.026,0.028)	0.923
		Enlisted Flyer	1.140	1.123	0.016 (-0.026,0.058)	0.449
		Enlisted Groundcrew	1.163	1.163	0.001 (-0.025,0.026)	0.964
15-33	Hyperemic Pressure Index (2 Minutes Post-exercise)	All	1.227	1.228	-0.002 (-0.017,0.014)	0.840
		Officer	1.250	1.253	-0.003 (-0.028,0.021)	0.797
		Enlisted Flyer	1.200	1.191	0.009 (-0.029,0.047)	0.654
		Enlisted Groundcrew	1.216	1.220	-0.004 (-0.027,0.019)	0.742
16-3	RBC Count (million/mm^3)	All	4.98	4.98	0.00 (-0.04,0.04)	0.937
		Officer	4.88	4.89	-0.01 (-0.08,0.05)	0.704
		Enlisted Flyer	4.98	5.01	-0.03 (-0.13,0.08)	0.600
		Enlisted Groundcrew	5.07	5.05	0.02 (-0.04,0.09)	0.505
16-5	WBC Count (thousand/mm^3)[a]	All	6.24	6.12	0.12	0.141
		Officer	5.91	5.88	0.03	0.826
		Enlisted Flyer	6.37	6.13	0.24	0.221
		Enlisted Groundcrew	6.51	6.33	0.17	0.171
16-7	Hemoglobin (gm/dL)	All	15.30	15.26	0.04 (-0.07,0.15)	0.505
		Officer	15.13	15.12	0.01 (-0.17,0.19)	0.916
		Enlisted Flyer	15.28	15.38	-0.10 (-0.37,0.17)	0.483
		Enlisted Groundcrew	15.46	15.34	0.12 (-0.05,0.29)	0.164
16-9	Hematocrit (percent)	All	45.83	45.70	0.13 (-0.22,0.49)	0.459
		Officer	45.21	45.19	0.02 (-0.54,0.58)	0.940
		Enlisted Flyer	45.92	46.10	-0.18 (-1.05,0.68)	0.681
		Enlisted Groundcrew	46.37	46.00	0.37 (-0.16,0.90)	0.175
16-11	Platelet Count (thousand/mm^3)[b]	All	237.6	234.4	3.2	0.247
		Officer	223.7	231.2	-7.5	0.077
		Enlisted Flyer	244.3	226.1	18.2	0.006
		Enlisted Groundcrew	247.9	240.2	7.7	0.064

Table Ref.	Clinical Parameter (Units)	Occupational Category	Mean Ranch Hand	Mean Comparison	Difference of Means (95% C.I.)	p-Value
16-14	Absolute Neutrophils (Segs) (thousand/mm^3)^b	All	3.68	3.61	0.07	0.213
		Officer	3.50	3.45	0.05	0.598
		Enlisted Flyer	3.82	3.67	0.14	0.324
		Enlisted Groundcrew	3.80	3.73	0.07	0.411
16-15	Absolute Neutrophils (Bands) (thousand/ mm^3) (Nonzero Measurements)^a	All	0.174	0.168	0.007	0.350
		Officer	0.169	0.165	0.004	0.720
		Enlisted Flyer	0.190	0.162	0.029	0.123
		Enlisted Groundcrew	0.174	0.172	0.001	0.895
16-17	Absolute Lymphocytes (thousand/mm^3)^a	All	1.64	1.63	0.01	0.778
		Officer	1.53	1.54	-0.01	0.845
		Enlisted Flyer	1.60	1.65	-0.05	0.481
		Enlisted Groundcrew	1.77	1.71	0.06	0.245
16-18	Absolute Monocytes (thousand/mm^3)^b	All	0.423	0.416	0.007	0.487
		Officer	0.408	0.404	0.004	0.807
		Enlisted Flyer	0.429	0.404	0.025	0.311
		Enlisted Groundcrew	0.434	0.430	0.004	0.803
16-19	Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements)^a	All	0.161	0.155	0.006	0.318
		Officer	0.147	0.150	-0.003	0.706
		Enlisted Flyer	0.180	0.162	0.018	0.221
		Enlisted Groundcrew	0.167	0.158	0.010	0.257
16-21	Absolute Basophils (thousand/mm^3) (Nonzero Measurements)^a	All	0.074	0.078	-0.003	0.102
		Officer	0.070	0.076	-0.006	0.060
		Enlisted Flyer	0.075	0.079	-0.004	0.476
		Enlisted Groundcrew	0.078	0.079	-0.000	0.927
16-23	Fibrinogen (mg/dL)^a	All	357.0	353.9	3.0	0.300
		Officer	350.9	345.2	5.7	0.207
		Enlisted Flyer	361.5	367.1	-5.5	0.450
		Enlisted Groundcrew	360.8	357.1	3.6	0.417
16-25	Erythrocyte Sedimentation Rate (mm/hr)^c	All	7.76	7.25	0.51	0.131
		Officer	7.35	6.65	0.71	0.156
		Enlisted Flyer	8.46	8.26	0.20	0.827
		Enlisted Groundcrew	7.87	7.47	0.40	0.439
17-5	Blood Urea Nitrogen (mg/dL)^a	All	16.18	16.52	-0.34	0.127
		Officer	16.84	17.48	-0.64	0.083
		Enlisted Flyer	16.19	16.29	-0.10	0.852
		Enlisted Groundcrew	15.60	15.80	-0.20	0.528
17-6	Serum Creatinine (mg/dL)^a	All	1.11	1.13	-0.02	0.038
		Officer	1.11	1.15	-0.03	0.025
		Enlisted Flyer	1.13	1.12	0.01	0.669
		Enlisted Groundcrew	1.09	1.11	-0.02	0.197
17-7	Creatinine Clearance^b	All	87.57	86.45	1.13	0.278
		Officer	82.88	80.92	1.96	0.210
		Enlisted Flyer	82.67	85.79	-3.12	0.202
		Enlisted Groundcrew	93.97	91.68	2.29	0.146

Table Ref.	Clinical Parameter (Units)	Occupational Category	Mean		Difference of Means (95% C.I.)		p-Value
			Ranch Hand	Comparison			
17-8	Urinary Microalbumin to Urinary Creatinine Ratio (µg/mg) (Nonzero Measurements)[a]	All	17.53	29.46	-11.93		0.008
		Officer	26.18	25.22	0.96		0.916
		Enlisted Flyer	20.40	37.07	-16.67		0.174
		Enlisted Groundcrew	12.68	30.16	-17.48		0.002
17-10	Urine Specific Gravity	All	1.0184	1.0184	0.0000	(-0.0006,0.0006)	0.979
		Officer	1.0173	1.1073	0.0000	(-0.0009,0.0009)	0.972
		Enlisted Flyer	1.0175	1.0189	-0.0014	(-0.0028,0.0000)	0.052
		Enlisted Groundcrew	1.0197	1.0192	0.0005	(-0.0003,0.0014)	0.224
18-12	TSH (µIU/mL)[a]	All	1.829	1.721	0.108		0.023
		Officer	2.014	1.803	0.211		0.010
		Enlisted Flyer	1.694	1.797	-0.104		0.362
		Enlisted Groundcrew	1.733	1.630	0.102		0.128
18-14	Free T_4 (ng/dL)[a]	All	1.080	1.064	0.016		0.047
		Officer	1.076	1.071	0.005		0.700
		Enlisted Flyer	1.116	1.054	0.062		0.001
		Enlisted Groundcrew	1.069	1.062	0.007		0.531
18-17	Fasting Glucose (mg/dL)[a]	All	101.7	102.0	-0.3		0.757
		Officer	100.5	100.5	0.0		0.994
		Enlisted Flyer	102.6	103.8	-1.2		0.627
		Enlisted Groundcrew	102.6	102.8	-0.3		0.853
18-19	2-hour Postprandial Glucose (mg/dL) (Nondiabetics Only)[a]	All	106.5	107.7	-1.2		0.509
		Officer	109.6	104.8	4.8		0.100
		Enlisted Flyer	114.0	115.5	-1.5		0.763
		Enlisted Groundcrew	101.0	107.8	-6.7		0.013
18-22	Fasting Insulin (µIU/mL)[a]	All	11.16	10.81	0.35		0.239
		Officer	10.38	9.85	0.53		0.219
		Enlisted Flyer	10.98	11.61	-0.63		0.400
		Enlisted Groundcrew	11.99	11.44	0.55		0.244
18-24	2-hour Postprandial Insulin (µIU/mL) (Nondiabetics Only)[a]	All	57.77	58.83	-1.07		0.647
		Officer	54.23	50.82	3.41		0.298
		Enlisted Flyer	66.41	66.77	-0.36		0.956
		Enlisted Groundcrew	58.16	64.38	-6.22		0.090
18-26	Hemoglobin A1c (percent) (Diabetics Only)[a]	All	6.68	6.67	0.01		0.962
		Officer	6.34	6.42	-0.08		0.706
		Enlisted Flyer	6.81	6.64	0.17		0.595
		Enlisted Groundcrew	6.91	6.88	0.03		0.870
18-28	C-peptide (ng/mL) (Diabetics Only)[b]	All	3.80	3.77	0.02		0.900
		Officer	4.04	3.64	0.40		0.236
		Enlisted Flyer	3.44	3.89	-0.44		0.313
		Enlisted Groundcrew	3.77	3.82	-0.06		0.852

Table Ref.	Clinical Parameter (Units)	Occupational Category	Mean		Difference of Means (95% C.I.)	p-Value
			Ranch Hand	Comparison		
18-30	Proinsulin (pmol/L) (Diabetics Only)[a]	All	24.44	23.37	1.07	0.719
		Officer	21.38	20.30	1.08	0.805
		Enlisted Flyer	26.33	24.25	2.08	0.770
		Enlisted Groundcrew	26.35	25.54	0.82	0.866
18-33	Total Testosterone (ng/dL)[b]	All	409.6	408.0	1.6	0.860
		Officer	395.5	399.5	-4.0	0.776
		Enlisted Flyer	424.3	409.6	14.8	0.508
		Enlisted Groundcrew	416.7	414.9	1.8	0.898
18-35	Free Testosterone (pg/mL)[b]	All	10.42	10.46	-0.03	0.853
		Officer	9.67	10.08	-0.42	0.133
		Enlisted Flyer	10.52	10.07	0.45	0.306
		Enlisted Groundcrew	11.09	10.92	0.17	0.549
18-37	Estradiol (pg/mL) (Measurements Above Sensitivity Limit)[a]	All	22.06	21.65	0.41	0.526
		Officer	22.09	21.58	0.50	0.629
		Enlisted Flyer	22.14	22.28	-0.15	0.927
		Enlisted Groundcrew	22.01	21.49	0.52	0.595
18-39	LH (mIU/mL)[a]	All	4.56	4.36	0.20	0.125
		Officer	4.83	4.37	0.46	0.034
		Enlisted Flyer	4.49	4.52	-0.03	0.925
		Enlisted Groundcrew	4.35	4.29	0.06	0.741
18-41	FSH (mIU/mL)[a]	All	5.78	5.68	0.11	0.562
		Officer	6.44	5.82	0.63	0.043
		Enlisted Flyer	5.56	5.79	-0.23	0.607
		Enlisted Groundcrew	5.32	5.52	-0.19	0.452
19-4	CD3+ Cells (T Cells) (cells/mm^3)[a]	All	1,234.5	1,203.0	31.5	0.402
		Officer	1,178.5	1,122.3	56.2	0.314
		Enlisted Flyer	1,168.9	1,236.9	-68.0	0.443
		Enlisted Groundcrew	1,329.2	1,253.8	75.5	0.216
19-5	CD4+ Cells (Helper T Cells) (cells/mm^3)[b]	All	887.8	872.1	15.7	0.553
		Officer	855.4	824.8	30.7	0.453
		Enlisted Flyer	824.8	884.3	-59.4	0.343
		Enlisted Groundcrew	951.7	903.8	47.9	0.252
19-6	CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]	All	527.1	517.5	9.5	0.629
		Officer	496.5	486.1	10.4	0.722
		Enlisted Flyer	540.9	560.8	-19.9	0.690
		Enlisted Groundcrew	556.9	525.6	31.3	0.318
19-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]	All	222.2	223.7	-1.5	0.873
		Officer	215.6	220.2	-4.6	0.745
		Enlisted Flyer	225.4	241.2	-15.9	0.493
		Enlisted Groundcrew	228.4	219.6	8.8	0.538
19-8	CD20+ Cells (B Cells) (cells/mm^3)[a]	All	181.3	189.4	-8.1	0.388
		Officer	161.4	167.0	-5.6	0.666
		Enlisted Flyer	167.7	186.7	-18.9	0.373
		Enlisted Groundcrew	212.8	209.4	3.4	0.834

Table Ref.	Clinical Parameter (Units)	Occupational Category	Mean		Difference of Means (95% C.I.)	p-Value
			Ranch Hand	Comparison		
19-9	CD3+CD4+ Cells (Helper Cells) (cells/mm^3)[b]	All	820.9	804.0	16.9	0.506
		Officer	789.5	757.9	31.7	0.419
		Enlisted Flyer	761.5	815.8	-54.3	0.366
		Enlisted Groundcrew	882.1	834.9	47.2	0.239
19-10	Absolute Lymphocytes (cells/mm^3)[a]	All	1,665.7	1,652.6	13.2	0.684
		Officer	1,538.2	1,552.8	-14.6	0.759
		Enlisted Flyer	1,662.9	1,665.6	-2.8	0.972
		Enlisted Groundcrew	1,792.3	1,739.0	53.3	0.298
19-11	IgA (mg/dL)[b]	All	254.8	258.3	-3.5	0.549
		Officer	247.3	248.0	-0.7	0.942
		Enlisted Flyer	253.6	260.2	-6.7	0.648
		Enlisted Groundcrew	262.1	266.7	-4.6	0.612
19-12	IgG (mg/dL)[a]	All	1,046.1	1,065.9	-19.8	0.131
		Officer	1,010.2	1,039.0	-28.8	0.155
		Enlisted Flyer	1,050.0	1,082.2	-32.1	0.327
		Enlisted Groundcrew	1,078.4	1,084.0	-5.7	0.779
19-13	IgM (mg/dL)[a]	All	89.15	91.40	-2.25	0.403
		Officer	85.43	88.05	-2.62	0.523
		Enlisted Flyer	82.99	98.53	-15.54	0.020
		Enlisted Groundcrew	95.26	91.97	3.29	0.431
20-8	FVC (percent of predicted)	All	100.84	101.65	-0.81 (-2.32,0.70)	0.293
		Officer	103.34	103.60	-0.26 (-2.65,2.13)	0.830
		Enlisted Flyer	99.18	100.87	-1.69 (-5.40,2.02)	0.372
		Enlisted Groundcrew	99.21	100.20	-0.99 (-3.26,1.28)	0.393
20-10	FEV$_1$ (percent of predicted)	All	88.18	89.40	-1.22 (-2.81,0.38)	0.136
		Officer	89.72	91.20	-1.48 (-4.00,1.05)	0.252
		Enlisted Flyer	84.49	86.37	-1.87 (-5.79,2.04)	0.349
		Enlisted Groundcrew	88.21	88.87	-0.66 (-3.05,1.74)	0.591
20-12	Ratio of Observed FEV$_1$ to Observed FVC[d]	All	0.713	0.717	-0.004	0.358
		Officer	0.701	0.712	-0.011	0.091
		Enlisted Flyer	0.700	0.697	0.002	0.825
		Enlisted Groundcrew	0.729	0.728	0.001	0.836

[a]Means transformed from natural logarithm scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm scale; p-value based on difference of means on natural logarithm scale.

[b]Means transformed from square root scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on square root scale; p-value based on difference of means on square root scale.

[c]Means transformed from natural logarithm (clinical parameter + 0.1) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (clinical parameter + 0.1) scale; p-value based on difference of means on natural logarithm (clinical parameter + 0.1) scale.

[d]Means transformed from natural logarithm (1 – clinical parameter) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (1 – clinical parameter) scale; p-value based on difference of means on natural logarithm (1 – clinical parameter) scale.

Table G-2. Summary of Unadjusted Results for Continuous Variables – Model 2 (Ranch Hands: Log$_2$ (Initial Dioxin))

Table Ref.	Clinical Parameter (Units)	R^2	Slope (Standard Error)[a]	p-Value[a]
9-6	Body Mass Index (kg/m^2)[b]	0.004	0.007 (0.006)*	0.203*
10-37	PSA (ng/mL)[b]	0.034	-0.064 (0.029)	0.027
12-20	WMS-R: Verbal Paired Associates	0.001	-0.074 (0.122)	0.546
12-21	WMS-R: Logical Memory, Immediate Recall	0.007	-0.207 (0.123)	0.095
12-22	WMS-R: Logical Memory, Delayed Recall	0.005	-0.185 (0.140)	0.188
12-23	WMS-R: Visual Reproduction, Immediate Recall	0.001	-0.053 (0.187)	0.777
12-24	WMS-R: Visual Reproduction, Delayed Recall	0.002	0.035 (0.237)	0.884
13-11	AST (U/L)[b]	0.003	-0.009 (0.012)	0.451
13-13	ALT (U/L)[b]	0.006	0.008 (0.010)	0.398
13-15	GGT (U/L)[b]	0.001	-0.008 (0.019)	0.676
13-17	Alkaline Phosphatase (U/L)[b]	0.005	0.010 (0.010)	0.282
13-19	Total Bilirubin (mg/dL)[b]	0.010	-0.035 (0.017)	0.044
13-22	LDH (U/L)[b]	0.008	-0.011 (0.007)	0.085
13-24	Cholesterol (mg/dL)[c]	0.042	0.026 (0.047)	0.586
13-26	HDL Cholesterol (mg/dL)[b]	0.075	-0.024 (0.009)	0.012
13-28	Cholesterol-HDL Ratio[b]	0.025	0.027 (0.010)	0.009
13-30	Triglycerides (mg/dL)[b]	0.018	0.036 (0.021)	0.084
13-32	Creatine Phosphokinase (U/L)[b]	0.012	0.000 (0.020)	0.994
13-34	Serum Amylase (U/L)[b]	0.039	-0.025 (0.015)	0.080
13-40	Prealbumin (mg/dL)[c]	0.059	-0.043 (0.021)	0.042
13-42	Albumin (mg/dL)	0.025	-9.287 (9.466)	0.327
13-44	α-1-Acid Glycoprotein (mg/dL)[b]	0.009	-0.013 (0.009)	0.145
13-46	α-1-Antitrypsin (mg/dL)[c]	0.001	0.010 (0.039)	0.797
13-48	α-2-Macroglobulin (mg/dL)[b]	0.018	-0.013 (0.012)	0.267
13-50	Apolipoprotein B (mg/dL)[c]	0.015	0.034 (0.042)	0.419
13-52	C3 Complement (mg/dL)[c]	0.045	0.037 (0.033)	0.274
13-54	C4 Complement (mg/dL)[c]	0.004	-0.026 (0.022)	0.230
13-56	Haptoglobin (mg/dL)[c]	0.009	-0.004 (0.099)	0.967
13-58	Transferrin (mg/dL)[b]	0.002	0.005 (0.006)	0.390
13-60	Prothrombin Time (seconds)[b]	0.013	-0.001 (0.002)	0.524
14-11	Duration of Post-SEA Acne (months) (Excluding Participants with Pre-SEA Acne)[c]	0.302	1.991 (0.423)	<0.001
14-12	Duration of Post-SEA Acne (months) (All Post-SEA Occurrences)[c]	0.040	0.903 (0.420)	0.034
15-7	Systolic Blood Pressure (mm Hg)[b]	0.011	0.000 (0.005)	0.985
15-9	Diastolic Blood Pressure (mm Hg)[c]	0.006	0.021 (0.020)	0.305
15-29	Resting Pressure Index	0.005	-0.003 (0.006)	0.569
15-31	Hyperemic Pressure Index (1 Minute Post-exercise)	0.003	-0.007 (0.007)	0.349
15-33	Hyperemic Pressure Index (2 Minutes Post-exercise)	0.004	-0.007 (0.006)	0.296
16-3	RBC Count (million/mm^3)	0.001	0.010 (0.016)	0.560
16-5	WBC Count (thousand/mm^3)[b]	0.009	0.012 (0.010)	0.210
16-7	Hemoglobin (gm/dL)	0.022	0.046 (0.044)	0.296
16-9	Hematocrit (percent)	0.016	0.094 (0.139)	0.497
16-11	Platelet Count (thousand/mm^3)[c]	0.033	0.148 (0.065)	0.024
16-14	Absolute Neutrophils (Segs) (thousand/mm^3)[c]	0.005	0.001 (0.012)	0.925

Table Ref.	Clinical Parameter (Units)	R^2	Slope (Standard Error)[a]	p-Value[a]
16-15	Absolute Neutrophils (Bands) (thousand/mm^3) (Nonzero Measurements)[b]	0.001	-0.022 (0.035)	0.539
16-17	Absolute Lymphocytes (thousand/mm^3)[b]	0.017	0.039 (0.015)	0.008
16-18	Absolute Monocytes (thousand/mm^3)[c]	0.004	0.007 (0.006)	0.234
16-19	Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements)[b]	<0.001	-0.004 (0.028)	0.882
16-21	Absolute Basophils (thousand/mm^3) (Nonzero Measurements)[b]	0.004	0.021 (0.023)	0.370
16-23	Fibrinogen (mg/dL)[b]	0.025	-0.001 (0.007)	0.840
16-25	Erythrocyte Sedimentation Rate (mm/hr)[d]	0.031	-0.004 (0.033)	0.904
17-5	Blood Urea Nitrogen (mg/dL)[b]	0.036	-0.014 (0.010)	0.185
17-6	Serum Creatinine (mg/dL)[b]	0.025	-0.016 (0.006)	0.010
17-7	Creatinine Clearance[c]	0.166	0.132 (0.040)	0.001
17-8	Urinary Microalbumin to Urinary Creatinine Ratio (µg/mg) (Nonzero Measurements)[b]	0.109	0.038 (0.132)	0.776
17-10	Urine Specific Gravity	0.006	0.0002 (0.0002)	0.409
18-12	TSH (µIU/mL)[b]	0.014	-0.012 (0.020)	0.541
18-14	Free T$_4$ (ng/dL)[b]	0.017	-0.005 (0.006)	0.392
18-17	Fasting Glucose (mg/dL)[b]	0.101	0.014 (0.008)	0.079
18-19	2-hour Postprandial Glucose (mg/dL) (Nondiabetics Only)[b]	0.039	-0.020 (0.015)	0.176
18-22	Fasting Insulin (µIU/mL)[b]	0.143	0.047 (0.021)	0.030
18-24	2-hour Postprandial Insulin (µIU/mL) (Nondiabetics Only)[b]	0.067	0.032 (0.034)	0.352
18-26	Hemoglobin A1c (percent) (Diabetics Only)[b]	0.063	0.032 (0.013)	0.014
18-28	C-peptide (ng/mL) (Diabetics Only)[c]	0.165	-0.088 (0.032)	0.007
18-30	Proinsulin (pmol/L) (Diabetics Only)[b]	0.073	-0.089 (0.080)	0.268
18-33	Total Testosterone (ng/dL)[c]	0.109	0.367 (0.163)	0.025
18-35	Free Testosterone (pg/mL)[c]	0.089	0.038 (0.020)	0.061
18-37	Estradiol (pg/mL) (Measurements Above Sensitivity Limit)[b]	0.001	-0.005 (0.023)	0.844
18-39	LH (mIU/mL)[b]	0.025	-0.051 (0.022)	0.020
18-41	FSH (mIU/mL)[b]	0.035	-0.061 (0.024)	0.011
19-4	CD3+ Cells (T Cells) (cells/mm^3)[b]	0.008	0.025 (0.027)	0.362
19-5	CD4+ Cells (Helper T Cells) (cells/mm^3)[c]	0.016	0.354 (0.371)	0.341
19-6	CD8+ Cells (Suppressor Cells) (cells/mm^3)[b]	0.010	0.010 (0.027)	0.703
19-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[b]	0.021	-0.035 (0.035)	0.328
19-8	CD20+ Cells (B Cells) (cells/mm^3)[b]	0.107	0.119 (0.035)	0.001
19-9	CD3+CD4+ Cells (Helper Cells) (cells/mm^3)[c]	0.018	0.409 (0.373)	0.274
19-10	Absolute Lymphocytes (cells/mm^3)[b]	0.013	0.031 (0.014)	0.029
19-11	IgA (mg/dL)[c]	0.004	0.089 (0.140)	0.526
19-12	IgG (mg/dL)[b]	<0.001	0.001 (0.010)	0.956
19-13	IgM (mg/dL)[b]	0.001	0.007 (0.023)	0.760
20-8	FVC (percent of predicted)	0.034	0.269 (0.543)	0.621
20-10	FEV$_1$ (percent of predicted)	0.006	0.929 (0.602)	0.124
20-12	Ratio of Observed FEV$_1$ to Observed FVC[e]	0.043	-0.032 (0.011)	0.004

[a]Adjusted for body mass index at the time of the blood measurement for dioxin.
[b]Slope and standard error based on natural logarithm of clinical parameter versus log$_2$ (initial dioxin).
[c]Slope and standard error based on square root of clinical parameter versus log$_2$ (initial dioxin).
[d]Slope and standard error based on natural logarithm of (clinical parameter + 0.1) versus log$_2$ (initial dioxin).
[e]Slope and standard error based on natural logarithm of (1 – clinical parameter) versus log$_2$ (initial dioxin).

*: Not adjusted for body mass index at the time of the blood measurement for dioxin.

Table G-3. Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)[a]	p-Value[a]
9-6	Body Mass Index (kg/m^2)[b]	0.027	Comparison	1,174	28.70*		
			Background RH	351	27.50*	-1.20*	<0.001*
			Low RH	211	29.51*	0.81*	0.010*
			High RH	213	29.90*	1.20*	<0.001*
			Low plus High RH	424	29.70*	1.00*	<0.001*
10-37	PSA (ng/mL)[b]	0.008	Comparison	1,089	0.97		
			Background RH	325	0.94	-0.03	0.575
			Low RH	187	1.07	0.10	0.129
			High RH	201	0.86	-0.11	0.062
			Low plus High RH	388	0.96	-0.01	0.781
12-20	WMS-R: Verbal Paired Associates	0.002	Comparison	1,169	10.96		
			Background RH	351	11.24	0.28 (-0.10,0.67)	0.154
			Low RH	211	10.82	-0.14 (-0.61,0.33)	0.567
			High RH	210	10.86	-0.10 (-0.58,0.37)	0.664
			Low plus High RH	421	10.84	-0.12 (-0.48,0.24)	0.507
12-21	WMS-R: Logical Memory, Immediate Recall	0.004	Comparison	1,169	11.58		
			Background RH	351	11.96	0.38 (-0.02,0.78)	0.060
			Low RH	211	11.78	0.20 (-0.29,0.68)	0.422
			High RH	210	11.20	-0.38 (-0.87,0.11)	0.126
			Low plus High RH	421	11.49	-0.09 (-0.46,0.28)	0.632
12-22	WMS-R: Logical Memory, Delayed Recall	0.004	Comparison	1,168	9.40		
			Background RH	351	9.89	0.49 (0.06,0.93)	0.027
			Low RH	211	9.58	0.18 (-0.35,0.71)	0.509
			High RH	210	9.13	-0.27 (-0.81,0.27)	0.328
			Low plus High RH	421	9.36	-0.04 (-0.45,0.36)	0.835
12-23	WMS-R: Visual Reproduction, Immediate Recall	0.007	Comparison	1,167	27.85		
			Background RH	351	28.20	0.36 (-0.22,0.94)	0.226
			Low RH	211	27.65	-0.19 (-0.90,0.51)	0.589
			High RH	210	27.81	-0.03 (-0.74,0.68)	0.925
			Low plus High RH	421	27.73	-0.11 (-0.65,0.42)	0.676
12-24	WMS-R: Visual Reproduction, Delayed Recall	0.005	Comparison	1,167	26.10		
			Background RH	351	26.72	0.62 (-0.14,1.39)	0.112
			Low RH	211	26.01	-0.08 (-1.02,0.85)	0.861
			High RH	210	26.05	-0.05 (-0.99,0.89)	0.922
			Low plus High RH	421	26.03	-0.07 (-0.78,0.65)	0.858
13-11	AST (U/L)[b]	<0.001	Comparison	1,154	24.17		
			Background RH	348	24.43	0.26	0.578
			Low RH	208	24.86	0.69	0.235
			High RH	211	24.22	0.05	0.930
			Low plus High RH	419	24.54	0.37	0.404

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)[a]	p-Value[a]
13-13	ALT (U/L)[b]	0.003	Comparison	1,154	44.59		
			Background RH	348	44.01	-0.58	0.433
			Low RH	208	45.16	0.57	0.529
			High RH	211	45.74	1.15	0.209
			Low plus High RH	419	45.45	0.86	0.214
13-15	GGT (U/L)[b]	0.007	Comparison	1,154	45.40		
			Background RH	348	42.90	-2.50	0.079
			Low RH	208	47.04	1.64	0.368
			High RH	211	47.90	2.50	0.172
			Low plus High RH	419	47.47	2.07	0.135
13-17	Alkaline Phosphatase (U/L)[b]	0.004	Comparison	1,154	92.33		
			Background RH	348	93.16	0.83	0.582
			Low RH	208	95.32	2.99	0.108
			High RH	211	96.02	3.69	0.048
			Low plus High RH	419	95.67	3.34	0.018
13-19	Total Bilirubin (mg/dL)[b]	0.002	Comparison	1,154	0.518		
			Background RH	348	0.531	0.013	0.394
			Low RH	208	0.525	0.007	0.681
			High RH	211	0.491	-0.027	0.154
			Low plus High RH	419	0.508	-0.010	0.500
13-22	LDH (U/L)[b]	0.014	Comparison	1,154	151.8		
			Background RH	348	154.7	2.9	0.094
			Low RH	208	155.5	3.7	0.078
			High RH	211	152.2	0.4	0.878
			Low plus High RH	419	153.8	2.0	0.210
13-24	Cholesterol (mg/dL)[c]	0.033	Comparison	1,154	197.7		
			Background RH	348	193.0	-4.7	0.035
			Low RH	208	195.1	-2.6	0.340
			High RH	211	196.9	-0.8	0.777
			Low plus High RH	419	196.0	-1.7	0.417
13-26	HDL Cholesterol (mg/dL)[b]	0.079	Comparison	1,154	44.65		
			Background RH	348	45.41	0.76	0.279
			Low RH	208	44.57	-0.08	0.925
			High RH	211	42.10	-2.55	0.002
			Low plus High RH	419	43.31	-1.34	0.035
13-28	Cholesterol-HDL Ratio[b]	0.025	Comparison	1,154	4.39		
			Background RH	348	4.22	-0.17	0.020
			Low RH	208	4.34	-0.05	0.627
			High RH	211	4.63	0.24	0.010
			Low plus High RH	419	4.49	0.10	0.163
13-30	Triglycerides (mg/dL)[b]	0.033	Comparison	1,154	133.3		
			Background RH	348	125.1	-8.2	0.045
			Low RH	208	138.2	4.9	0.357
			High RH	211	149.9	16.6	0.002
			Low plus High RH	419	143.9	10.6	0.009

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)[a]	p-Value[a]
13-32	Creatine Phosphokinase (U/L)[b]	0.028	Comparison	1,154	106.1		
			Background RH	348	106.0	-0.1	0.964
			Low RH	208	110.4	4.3	0.382
			High RH	211	109.3	3.2	0.514
			Low plus High RH	419	109.8	3.7	0.315
13-34	Serum Amylase (U/L)[b]	0.035	Comparison	1,154	55.54		
			Background RH	348	54.26	-1.28	0.322
			Low RH	208	55.96	0.42	0.794
			High RH	211	52.59	-2.95	0.057
			Low plus High RH	419	54.24	-1.30	0.277
13-40	Prealbumin (mg/dL)[c]	0.018	Comparison	1,154	28.81		
			Background RH	348	28.85	0.04	0.923
			Low RH	208	29.21	0.40	0.355
			High RH	211	28.98	0.17	0.699
			Low plus High RH	419	29.10	0.29	0.389
13-42	Albumin (mg/dL)	0.008	Comparison	1,154	4,187.4		
			Background RH	348	4,172.6	-14.8 (-47.9,18.4)	0.383
			Low RH	208	4,198.8	11.4 (-29.2,51.9)	0.583
			High RH	211	4,201.4	14.0 (-26.5,54.4)	0.499
			Low plus High RH	419	4,200.1	12.7 (-18.1,43.5)	0.420
13-44	α-1-Acid Glycoprotein (mg/dL)[b]	0.004	Comparison	1,154	78.09		
			Background RH	348	76.62	-1.47	0.200
			Low RH	208	80.71	2.62	0.069
			High RH	211	79.33	1.24	0.384
			Low plus High RH	419	80.01	1.92	0.078
13-46	α-1-Antitrypsin (mg/dL)[c]	0.004	Comparison	1,154	140.2		
			Background RH	348	139.8	-0.4	0.781
			Low RH	208	144.3	4.1	0.037
			High RH	211	143.4	3.2	0.106
			Low plus High RH	419	143.8	3.6	0.015
13-48	α-2-Macro-globulin (mg/dL)[b]	0.021	Comparison	1,154	185.9		
			Background RH	348	187.2	1.3	0.717
			Low RH	208	190.1	4.2	0.335
			High RH	211	179.4	-6.5	0.119
			Low plus High RH	419	184.7	-1.2	0.687
13-50	Apolipoprotein B (mg/dL)[c]	0.008	Comparison	1,154	103.1		
			Background RH	348	100.5	-2.6	0.073
			Low RH	208	102.7	-0.4	0.811
			High RH	211	104.0	0.9	0.616
			Low plus High RH	419	103.4	0.3	0.860
13-52	C3 Complement (mg/dL)[c]	0.080	Comparison	1,154	119.1		
			Background RH	348	116.6	-2.5	0.051
			Low RH	208	123.8	4.7	0.003
			High RH	211	122.3	3.2	0.038
			Low plus High RH	419	123.0	3.9	<0.001

Table G-3. Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)[a]	p-Value[a]
13-54	C4 Complement (mg/dL)[c]	0.008	Comparison	1,154	22.74		
			Background RH	348	22.14	-0.60	0.088
			Low RH	208	23.09	0.35	0.414
			High RH	211	22.24	-0.50	0.244
			Low plus High RH	419	22.66	-0.08	0.812
13-56	Haptoglobin (mg/dL)[c]	0.009	Comparison	1,154	119.0		
			Background RH	348	121.3	2.3	0.536
			Low RH	208	130.4	11.4	0.013
			High RH	211	132.8	13.8	0.003
			Low plus High RH	419	131.6	12.6	<0.001
13-58	Transferrin (mg/dL)[b]	0.009	Comparison	1,154	253.9		
			Background RH	348	250.2	-3.7	0.132
			Low RH	208	259.7	5.8	0.058
			High RH	211	260.0	6.1	0.046
			Low plus High RH	419	259.8	5.9	0.011
13-60	Prothrombin Time (seconds)[b]	0.007	Comparison	894	10.71		
			Background RH	269	10.79	0.08	0.025
			Low RH	145	10.73	0.02	0.522
			High RH	157	10.67	-0.04	0.482
			Low plus High RH	302	10.70	-0.01	0.950
14-11	Duration of Post-SEA Acne (months) (Excluding Participants with Pre-SEA Acne)[c]	0.087	Comparison	86	53.05		
			Background RH	32	46.99	-6.06	0.656
			Low RH	26	47.31	-5.74	0.697
			High RH	30	117.02	63.97	<0.001
			Low plus High RH	56	80.80	27.75	0.032
14-12	Duration of Post-SEA Acne (months) (All Post-SEA Occurrences)[c]	0.010	Comparison	231	134.52		
			Background RH	83	126.57	-7.95	0.676
			Low RH	57	99.05	-35.47	0.084
			High RH	61	151.32	16.80	0.450
			Low plus High RH	118	124.69	-9.83	0.554
15-7	Systolic Blood Pressure (mm Hg)[b]	0.019	Comparison	1,156	129.2		
			Background RH	347	129.0	-0.2	0.852
			Low RH	206	126.9	-2.3	0.074
			High RH	212	126.8	-2.4	0.057
			Low plus High RH	418	126.9	-2.3	0.015
15-9	Diastolic Blood Pressure (mm Hg)[c]	0.002	Comparison	1,156	75.02		
			Background RH	347	74.23	-0.79	0.185
			Low RH	206	74.48	-0.54	0.457
			High RH	212	75.75	0.73	0.312
			Low plus High RH	418	75.12	0.10	0.851

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)[a]	p-Value[a]
15-29	Resting Pressure Index	0.001	Comparison	1,138	1.254		
			Background RH	347	1.248	-0.005 (-0.023,0.012)	0.567
			Low RH	206	1.251	-0.003 (-0.024,0.019)	0.806
			High RH	209	1.252	-0.002 (-0.023,0.020)	0.885
			Low plus High RH	415	1.251	-0.002 (-0.019,0.014)	0.798
15-31	Hyperemic Pressure Index (1 Minute Post-exercise)	0.003	Comparison	1,108	1.172		
			Background RH	340	1.177	0.005 (-0.017,0.028)	0.642
			Low RH	199	1.179	0.006 (-0.021,0.034)	0.649
			High RH	200	1.169	-0.004 (-0.031,0.024)	0.803
			Low plus High RH	399	1.174	0.001 (-0.020,0.023)	0.893
15-33	Hyperemic Pressure Index (2 Minutes Post-exercise)	0.002	Comparison	1,110	1.229		
			Background RH	340	1.229	0.000 (-0.020,0.021)	0.988
			Low RH	199	1.227	-0.001 (-0.027,0.024)	0.914
			High RH	200	1.223	-0.005 (-0.030,0.020)	0.693
			Low plus High RH	399	1.225	-0.003 (-0.022,0.016)	0.741
16-3	RBC Count (million/mm^3)	0.001	Comparison	1,171	4.98		
			Background RH	351	4.96	-0.02 (-0.08,0.03)	0.391
			Low RH	210	4.99	0.01 (-0.05,0.08)	0.685
			High RH	209	5.00	0.02 (-0.05,0.09)	0.587
			Low plus High RH	419	5.00	0.02 (-0.04,0.07)	0.532
16-5	WBC Count (thousand/mm^3)[b]	0.004	Comparison	1,171	6.12		
			Background RH	351	6.16	0.04	0.691
			Low RH	210	6.25	0.13	0.297
			High RH	209	6.35	0.23	0.079
			Low plus High RH	419	6.30	0.18	0.065
16-7	Hemoglobin (gm/dL)	0.006	Comparison	1,171	15.26		
			Background RH	351	15.22	-0.04 (-0.19,0.11)	0.581
			Low RH	210	15.33	0.07 (-0.11,0.25)	0.470
			High RH	209	15.38	0.12 (-0.06,0.30)	0.188
			Low plus High RH	419	15.36	0.09 (-0.04,0.23)	0.179
16-9	Hematocrit (percent)	0.007	Comparison	1,171	45.70		
			Background RH	351	45.61	-0.09 (-0.56,0.38)	0.702
			Low RH	210	45.94	0.23 (-0.34,0.81)	0.421
			High RH	209	46.03	0.33 (-0.25,0.90)	0.262
			Low plus High RH	419	45.99	0.28 (-0.15,0.72)	0.205
16-11	Platelet Count (thousand/mm^3)[c]	0.027	Comparison	1,168	234.6		
			Background RH	350	232.1	-2.5	0.494
			Low RH	210	234.8	0.2	0.954
			High RH	209	248.3	13.7	0.002
			Low plus High RH	419	241.5	6.9	0.038

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)[a]	p-Value[a]
16-14	Absolute Neutrophils (Segs) (thousand/mm^3)[c]	0.004	Comparison	1,171	3.61		
			Background RH	351	3.61	0.00	0.980
			Low RH	210	3.77	0.16	0.094
			High RH	209	3.72	0.11	0.247
			Low plus High RH	419	3.74	0.13	0.062
16-15	Absolute Neutrophils (Bands) (thousand/mm^3) (Nonzero Measurements)[b]	0.003	Comparison	932	0.168		
			Background RH	291	0.166	-0.002	0.885
			Low RH	163	0.186	0.018	0.137
			High RH	171	0.178	0.010	0.390
			Low plus High RH	334	0.182	0.014	0.124
16-17	Absolute Lymphocytes (thousand/mm^3)[b]	0.004	Comparison	1,171	1.63		
			Background RH	351	1.61	-0.02	0.635
			Low RH	210	1.58	-0.05	0.316
			High RH	209	1.75	0.12	0.031
			Low plus High RH	419	1.66	0.03	0.448
16-18	Absolute Monocytes (thousand/mm^3)[c]	0.001	Comparison	1,171	0.416		
			Background RH	351	0.428	0.012	0.351
			Low RH	210	0.417	0.001	0.922
			High RH	209	0.419	0.003	0.819
			Low plus High RH	419	0.418	0.002	0.829
16-19	Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements)[b]	0.002	Comparison	1,045	0.155		
			Background RH	320	0.161	0.006	0.429
			Low RH	185	0.167	0.012	0.202
			High RH	193	0.155	0.000	0.940
			Low plus High RH	378	0.161	0.006	0.436
16-21	Absolute Basophils (thousand/mm^3) (Nonzero Measurements)[b]	0.005	Comparison	620	0.078		
			Background RH	181	0.072	-0.006	0.030
			Low RH	108	0.076	-0.002	0.610
			High RH	108	0.077	-0.001	0.859
			Low plus High RH	216	0.076	-0.002	0.650
16-23	Fibrinogen (mg/dL)[b]	0.019	Comparison	1,171	353.8		
			Background RH	350	353.2	-0.6	0.872
			Low RH	210	365.1	11.3	0.017
			High RH	209	355.8	2.0	0.674
			Low plus High RH	419	360.4	6.6	0.064
16-25	Erythrocyte Sedimentation Rate (mm/hr)[d]	0.028	Comparison	1,171	7.23		
			Background RH	351	7.26	0.03	0.939
			Low RH	210	8.56	1.33	0.018
			High RH	209	7.96	0.73	0.181
			Low plus High RH	419	8.25	1.02	0.015

Table G-3. Summary of Unadjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)[a]	p-Value[a]
17-5	Blood Urea Nitrogen (mg/dL)[b]	0.016	Comparison	1,174	16.51		
			Background RH	352	16.47	-0.04	0.877
			Low RH	211	16.26	-0.25	0.477
			High RH	213	15.81	-0.70	0.044
			Low plus High RH	424	16.03	0.48	0.072
17-6	Serum Creatinine (mg/dL)[b]	0.013	Comparison	1,174	1.13		
			Background RH	352	1.11	-0.02	0.251
			Low RH	211	1.13	0.00	0.886
			High RH	213	1.08	-0.05	0.003
			Low plus High RH	424	1.10	-0.03	0.060
17-7	Creatinine Clearance[c]	0.147	Comparison	1,174	86.31		
			Background RH	351	85.35	-0.96	0.446
			Low RH	211	86.40	0.09	0.959
			High RH	213	93.37	7.06	<0.001
			Low plus High RH	424	89.87	3.56	0.003
17-8	Urinary Microalbumin to Urinary Creatinine Ratio (µg/mg) (Nonzero Measurements)[b]	0.016	Comparison	141	28.54		
			Background RH	42	19.95	-8.59	0.173
			Low RH	35	16.05	-12.49	0.039
			High RH	29	18.89	-9.65	0.170
			Low plus High RH	64	17.28	-11.26	0.024
17-10	Urine Specific Gravity	0.005	Comparison	1,174	1.0184		
			Background RH	352	1.0180	-0.0004 (-0.0011,0.0004)	0.352
			Low RH	211	1.0185	0.0001 (-0.0008,0.0011)	0.778
			High RH	213	1.0189	0.0005 (-0.0004,0.0015)	0.245
			Low plus High RH	424	1.0187	0.0003 (-0.0004,0.0010)	0.341
18-12	TSH (µIU/mL)[b]	0.005	Comparison	1,089	1.721		
			Background RH	328	1.895	0.174	0.007
			Low RH	201	1.797	0.076	0.316
			High RH	203	1.764	0.043	0.564
			Low plus High RH	404	1.781	0.060	0.300
18-14	Free T$_4$ (ng/dL)[b]	0.006	Comparison	1,089	1.064		
			Background RH	328	1.081	0.017	0.102
			Low RH	201	1.076	0.012	0.342
			High RH	203	1.080	0.016	0.215
			Low plus High RH	404	1.078	0.014	0.150
18-17	Fasting Glucose (mg/dL)[b]	0.095	Comparison	1,173	101.9		
			Background RH	352	101.7	-0.2	0.834
			Low RH	210	102.1	0.2	0.923
			High RH	213	102.2	0.3	0.848
			Low plus High RH	423	102.2	0.3	0.849

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)[a]	p-Value[a]
18-19	2-hour Post-prandial Glucose (mg/dL) (Nondiabetics Only)[b]	0.031	Comparison	936	107.5		
			Background RH	308	108.0	0.5	0.832
			Low RH	161	108.3	0.8	0.808
			High RH	159	102.6	-4.9	0.102
			Low plus High RH	320	105.4	-2.1	0.359
18-22	Fasting Insulin (µIU/mL)[b]	0.139	Comparison	1,173	10.77		
			Background RH	352	10.69	-0.08	0.809
			Low RH	210	11.49	0.72	0.113
			High RH	213	11.98	1.21	0.009
			Low plus High RH	423	11.73	0.96	0.006
18-24	2-hour Post-prandial Insulin (µIU/mL) (Nondiabetics Only)[b]	0.068	Comparison	936	58.56		
			Background RH	308	55.88	-2.68	0.342
			Low RH	161	61.11	2.55	0.505
			High RH	159	60.12	1.56	0.684
			Low plus High RH	320	60.62	2.06	0.477
18-26	Hemoglobin A1c (percent) (Diabetics Only)[b]	0.011	Comparison	221	6.67		
			Background RH	42	6.50	-0.17	0.418
			Low RH	46	6.58	-0.09	0.661
			High RH	51	6.92	0.25	0.235
			Low plus High RH	97	6.76	0.09	0.605
18-28	C-peptide (ng/mL) (Diabetics Only)[c]	0.102	Comparison	221	3.78		
			Background RH	42	3.63	-0.15	0.599
			Low RH	46	4.25	0.47	0.108
			High RH	51	3.50	-0.28	0.292
			Low plus High RH	97	3.85	0.07	0.754
18-30	Proinsulin (pmol/L) (Diabetics Only)[b]	0.092	Comparison	221	23.51		
			Background RH	42	19.30	-4.21	0.292
			Low RH	46	26.11	2.60	0.560
			High RH	51	27.26	3.75	0.388
			Low plus High RH	97	26.71	3.20	0.345
18-33	Total Testosterone (ng/dL)[c]	0.096	Comparison	1,161	408.9		
			Background RH	349	406.7	-2.2	0.839
			Low RH	210	396.2	-12.7	0.350
			High RH	210	420.4	11.5	0.411
			Low plus High RH	420	408.2	-0.7	0.942
18-35	Free Testosterone (pg/mL)[c]	0.080	Comparison	1,161	10.47		
			Background RH	349	10.04	-0.43	0.055
			Low RH	210	10.41	-0.06	0.818
			High RH	210	10.95	0.48	0.090
			Low plus High RH	420	10.68	0.21	0.334

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)[a]	p-Value[a]
18-37	Estradiol (pg/mL) (Measurements Above Sensitivity Limit)[b]	0.001	Comparison	746	21.65		
			Background RH	221	22.52	0.87	0.320
			Low RH	139	21.89	0.24	0.814
			High RH	142	21.45	-0.20	0.846
			Low plus High RH	281	21.67	0.02	0.980
18-39	LH (mIU/mL)[b]	0.006	Comparison	1,161	4.35		
			Background RH	349	4.60	0.25	0.156
			Low RH	210	4.96	0.61	0.006
			High RH	210	4.12	-0.23	0.235
			Low plus High RH	420	4.52	0.17	0.307
18-41	FSH (mIU/mL)[b]	0.006	Comparison	1,161	5.68		
			Background RH	349	5.85	0.17	0.474
			Low RH	210	6.40	0.72	0.019
			High RH	210	5.15	-0.53	0.056
			Low plus High RH	420	5.74	0.06	0.774
19-4	CD3+ Cells (T Cells) (cells/mm^3)[b]	0.008	Comparison	422	1,203.0		
			Background RH	122	1,174.3	-28.7	0.558
			Low RH	72	1,235.5	32.5	0.598
			High RH	78	1,333.6	130.6	0.036
			Low plus High RH	150	1,285.6	82.6	0.080
19-5	CD4+ Cells (Helper T Cells) (cells/mm^3)[c]	0.008	Comparison	422	872.1		
			Background RH	122	843.7	-28.4	0.415
			Low RH	72	884.2	12.1	0.781
			High RH	78	962.5	90.4	0.036
			Low plus High RH	150	924.5	52.4	0.112
19-6	CD8+ Cells (Suppressor Cells) (cells/mm^3)[b]	0.002	Comparison	422	517.6		
			Background RH	122	508.2	-9.4	0.718
			Low RH	72	541.9	24.3	0.459
			High RH	78	543.7	26.1	0.412
			Low plus High RH	150	542.8	25.2	0.304
19-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[b]	0.006	Comparison	422	223.7		
			Background RH	122	213.6	-10.1	0.400
			Low RH	72	243.6	19.9	0.206
			High RH	78	217.5	-6.2	0.672
			Low plus High RH	150	229.7	6.0	0.599
19-8	CD20+ Cells (B Cells) (cells/mm^3)[b]	0.018	Comparison	422	189.4		
			Background RH	122	174.4	-15.0	0.219
			Low RH	72	155.3	-34.1	0.016
			High RH	78	222.1	32.7	0.047
			Low plus High RH	150	187.0	-2.4	0.839

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Mean[a]	Difference of Mean vs. Comparisons (95% C.I.)[a]	p-Value[a]
19-9	CD3+CD4+ Cells (Helper Cells) (cells/mm^3)[c]	0.009	Comparison	422	804.0		
			Background RH	122	781.4	-22.6	0.500
			Low RH	72	808.4	4.4	0.916
			High RH	78	896.5	92.5	0.026
			Low plus High RH	150	853.6	49.6	0.116
19-10	Absolute Lymphocytes (cells/mm^3)[b]	0.005	Comparison	1,068	1,652.7		
			Background RH	317	1,606.9	-45.8	0.276
			Low RH	187	1,645.2	-7.5	0.886
			High RH	190	1,782.3	129.6	0.017
			Low plus High RH	377	1,712.9	60.2	0.135
19-11	IgA (mg/dL)[c]	0.005	Comparison	1,068	258.1		
			Background RH	317	248.3	-9.8	0.205
			Low RH	187	264.3	6.2	0.521
			High RH	190	256.0	-2.1	0.830
			Low plus High RH	377	260.1	2.0	0.781
19-12	IgG (mg/dL)[b]	0.004	Comparison	1,068	1,065.7		
			Background RH	317	1,031.1	-34.6	0.045
			Low RH	187	1,068.6	2.9	0.892
			High RH	190	1,050.1	-15.6	0.467
			Low plus High RH	377	1,059.3	-6.4	0.694
19-13	IgM (mg/dL)[b]	0.004	Comparison	1,068	91.49		
			Background RH	317	88.61	-2.88	0.416
			Low RH	187	87.67	-3.82	0.378
			High RH	190	91.26	-0.23	0.957
			Low plus High RH	377	89.46	-2.03	0.540
20-8	FVC (percent of predicted)	0.066	Comparison	1,161	101.72		
			Background RH	348	102.68	0.95 (-0.98,2.89)	0.334
			Low RH	207	97.86	-3.86 (-6.23,-1.49)	0.001
			High RH	212	100.39	-1.33 (-3.69,1.03)	0.269
			Low plus High RH	419	99.14	-2.58 (-4.37,-0.78)	0.005
20-10	FEV$_1$ (percent of predicted)	0.011	Comparison	1,161	89.42		
			Background RH	348	89.24	-0.18 (-2.28,1.92)	0.869
			Low RH	207	85.31	-4.11 (-6.69,-1.53)	0.002
			High RH	212	89.24	-0.18 (-2.74,2.38)	0.890
			Low plus High RH	419	87.30	-2.12 (-4.07,-0.17)	0.033
20-12	Ratio of Observed FEV$_1$ to Observed FVC[e]	0.038	Comparison	1,161	0.717		
			Background RH	348	0.707	-0.010	0.056
			Low RH	207	0.709	-0.008	0.201
			High RH	212	0.730	0.013	0.027
			Low plus High RH	419	0.720	0.003	0.528

[a]Adjusted for body mass index at the time of the blood measurement for dioxin.

[b]Means transformed from natural logarithm scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm scale; p-value based on difference of means on natural logarithm scale.

[c]Means transformed from square root scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on square root scale; p-value based on difference of means on square root scale.

[d]Means transformed from natural logarithm (clinical parameter + 0.1) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (clinical parameter + 0.1) scale; p-value based on difference of means on natural logarithm (clinical parameter + 0.1) scale.

[e]Means transformed from natural logarithm (1 – clinical parameter) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (1 – clinical parameter) scale; p-value based on difference of means on natural logarithm (1 – clinical parameter) scale.

*: Not adjusted for body mass index at the time of the blood measurement for dioxin.

Note: RH = Ranch Hand.
    Background: (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table G-4. Summary of Unadjusted Results for Continuous Variables – Model 4 (Ranch Hands: Log$_2$ (1987 Dioxin))

Table Ref.	Clinical Parameter (Units)	R^2	Slope (Standard Error)[a]	p-Value
9-6	Body Mass Index (kg/m^2)[a]	0.066	0.024 (0.003)	<0.001
10-37	PSA (ng/mL)[a]	0.004	-0.029 (0.018)	0.113
12-20	WMS-R: Verbal Paired Associates	0.007	-0.168 (0.072)	0.020
12-21	WMS-R: Logical Memory, Immediate Recall	0.013	-0.237 (0.073)	0.001
12-22	WMS-R: Logical Memory, Delayed Recall	0.011	-0.237 (0.082)	0.004
12-23	WMS-R: Visual Reproduction, Immediate Recall	0.004	-0.183 (0.108)	0.090
12-24	WMS-R: Visual Reproduction, Delayed Recall	0.005	-0.272 (0.139)	0.051
13-11	AST (U/L)[a]	<0.001	-0.000 (0.008)	0.977
13-13	ALT (U/L)[a]	0.005	0.012 (0.006)	0.059
13-15	GGT (U/L)[a]	0.004	0.020 (0.011)	0.075
13-17	Alkaline Phosphatase (U/L)[a]	0.001	0.005 (0.006)	0.393
13-19	Total Bilirubin (mg/dL)[a]	0.005	-0.022 (0.011)	0.040
13-22	LDH (U/L)[a]	<0.001	-0.001 (0.004)	0.879
13-24	Cholesterol (mg/dL)[b]	<0.001	-0.001 (0.029)	0.979
13-26	HDL Cholesterol (mg/dL)[a]	0.032	-0.031 (0.006)	<0.001
13-28	Cholesterol-HDL Ratio[a]	0.028	0.030 (0.006)	<0.001
13-30	Triglycerides (mg/dL)[a]	0.031	0.060 (0.012)	<0.001
13-32	Creatine Phosphokinase (U/L)[a]	0.006	0.028 (0.013)	0.032
13-34	Serum Amylase (U/L)[a]	0.006	-0.019 (0.009)	0.029
13-40	Prealbumin (mg/dL)[b]	0.001	-0.014 (0.013)	0.299
13-42	Albumin (mg/dL)	<0.001	2.239 (6.214)	0.719
13-44	α-1-Acid Glycoprotein (mg/dL)[a]	0.002	0.006 (0.005)	0.245
13-46	α-1-Antitrypsin (mg/dL)[b]	0.003	0.037 (0.024)	0.120
13-48	α-2-Macroglobulin (mg/dL)[a]	0.001	-0.006 (0.007)	0.385
13-50	Apolipoprotein B (mg/dL)[b]	0.003	0.038 (0.026)	0.151
13-52	C3 Complement (mg/dL)[b]	0.045	0.126 (0.021)	<0.001
13-54	C4 Complement (mg/dL)[b]	0.002	0.016 (0.013)	0.227
13-56	Haptoglobin (mg/dL)[b]	0.004	0.108 (0.061)	0.076
13-58	Transferrin (mg/dL)[a]	0.019	0.013 (0.004)	<0.001
13-60	Prothrombin Time (seconds)[a]	0.007	-0.002 (0.001)	0.044
14-11	Duration of Post-SEA Acne (months) (Excluding Participants with Pre-SEA Acne)[b]	0.166	1.103 (0.267)	<0.001
14-12	Duration of Post-SEA Acne (months) (All Post-SEA Occurrences)[b]	0.006	0.298 (0.264)	0.259
15-7	Systolic Blood Pressure (mm Hg)[a]	<0.001	-0.001 (0.003)	0.652
15-9	Diastolic Blood Pressure (mm Hg)[b]	0.002	0.015 (0.012)	0.224
15-29	Resting Pressure Index	<0.001	-0.001 (0.003)	0.721
15-31	Hyperemic Pressure Index (1 Minute Post-exercise)	0.002	-0.005 (0.004)	0.228
15-33	Hyperemic Pressure Index (2 Minutes Post-exercise)	0.003	-0.005 (0.004)	0.142
16-3	RBC Count (million/mm^3)	0.003	0.016 (0.011)	0.130
16-5	WBC Count (thousand/mm^3)[a]	0.001	0.006 (0.006)	0.341
16-7	Hemoglobin (gm/dL)	0.002	0.032 (0.028)	0.246
16-9	Hematocrit (percent)	0.001	0.072 (0.089)	0.415
16-11	Platelet Count (thousand/mm^3)[b]	0.003	0.063 (0.042)	0.129
16-14	Absolute Neutrophils (Segs) (thousand/mm^3)[b]	0.001	0.008 (0.007)	0.302

Table Ref.	Clinical Parameter (Units)	R^2	Slope (Standard Error)[a]	p-Value
16-15	Absolute Neutrophils (Bands) (thousand/mm^3) (Nonzero Measurements)[a]	0.002	0.021 (0.021)	0.310
16-17	Absolute Lymphocytes (thousand/mm^3)[a]	0.004	0.016 (0.010)	0.099
16-18	Absolute Monocytes (thousand/mm^3)[b]	<0.001	0.002 (0.004)	0.602
16-19	Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements)[a]	<0.001	0.002 (0.017)	0.911
16-21	Absolute Basophils (thousand/mm^3) (Nonzero Measurements)[a]	0.016	0.035 (0.014)	0.012
16-23	Fibrinogen (mg/dL)[a]	0.007	0.009 (0.004)	0.021
16-25	Erythrocyte Sedimentation Rate (mm/hr)[c]	0.010	0.060 (0.021)	0.005
17-5	Blood Urea Nitrogen (mg/dL)[a]	<0.001	-0.003 (0.006)	0.628
17-6	Serum Creatinine (mg/dL)[a]	0.001	-0.004 (0.004)	0.326
17-7	Creatinine Clearance[b]	0.056	0.173 (0.026)	<0.001
17-8	Urinary Microalbumin to Urinary Creatinine Ratio (µg/mg) (Nonzero Measurements)[a]	0.007	0.073 (0.085)	0.390
17-10	Urine Specific Gravity	0.006	0.0003 (0.0001)	0.033
18-12	TSH (µIU/mL)[a]	0.001	-0.010 (0.013)	0.405
18-14	Free T$_4$ (ng/dL)[a]	0.001	-0.003 (0.003)	0.441
18-17	Fasting Glucose (mg/dL)[a]	0.016	0.016 (0.005)	<0.001
18-19	2-hour Postprandial Glucose (mg/dL) (Nondiabetics Only)[a]	<0.001	-0.005 (0.009)	0.601
18-22	Fasting Insulin (µIU/mL)[a]	0.040	0.077 (0.014)	<0.001
18-24	2-hour Postprandial Insulin (µIU/mL) (Nondiabetics Only)[a]	0.013	0.058 (0.020)	0.004
18-26	Hemoglobin A1c (percent) (Diabetics Only)[a]	0.037	0.023 (0.010)	0.023
18-28	C-peptide (ng/mL) (Diabetics Only)[b]	<0.001	0.000 (0.026)	0.998
18-30	Proinsulin (pmol/L) (Diabetics Only)[a]	0.013	0.086 (0.064)	0.180
18-33	Total Testosterone (ng/dL)[b]	0.004	-0.190 (0.107)	0.077
18-35	Free Testosterone (pg/mL)[b]	<0.001	-0.001 (0.013)	0.930
18-37	Estradiol (pg/mL) (Measurements Above Sensitivity Limit)[a]	<0.001	0.001 (0.014)	0.930
18-39	LH (mIU/mL)[a]	0.005	-0.026 (0.014)	0.057
18-41	FSH (mIU/mL)[a]	0.001	-0.015 (0.015)	0.309
19-4	CD3+ Cells (T Cells) (cells/mm^3)[a]	0.013	0.030 (0.016)	0.063
19-5	CD4+ Cells (Helper T Cells) (cells/mm^3)[b]	0.013	0.406 (0.218)	0.063
19-6	CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]	0.007	0.025 (0.019)	0.172
19-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]	0.003	0.018 (0.021)	0.379
19-8	CD20+ Cells (B Cells) (cells/mm^3)[a]	0.015	0.046 (0.022)	0.042
19-9	CD3+CD4+ Cells (Helper Cells) (cells/mm^3)[b]	0.012	0.389 (0.218)	0.075
19-10	Absolute Lymphocytes (cells/mm^3)[a]	0.007	0.021 (0.009)	0.029
19-11	IgA (mg/dL)[b]	0.004	0.147 (0.088)	0.096
19-12	IgG (mg/dL)[a]	0.002	0.007 (0.006)	0.275
19-13	IgM (mg/dL)[a]	<0.001	-0.002 (0.014)	0.902
20-8	FVC (percent of predicted)	0.020	-1.419 (0.356)	<0.001
20-10	FEV$_1$ (percent of predicted)	0.001	-0.287 (0.386)	0.457
20-12	Ratio of Observed FEV$_1$ to Observed FVC[d]	0.028	-0.031 (0.007)	<0.001

[a]Slope and standard error based on natural logarithm of clinical parameter versus log$_2$ (1987 dioxin).
[b]Slope and standard error based on square root of clinical parameter versus log$_2$ (1987 dioxin).
[c]Slope and standard error based on natural logarithm of (clinical parameter + 0.1) versus log$_2$ (1987 dioxin).
[d]Slope and standard error based on natural logarithm of (1 – clinical parameter) versus log$_2$ (1987 dioxin).

Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons)

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
9-3	Self-perception of Health	All	110 (14.2)	158 (13.5)	1.06 (0.81,1.38)	0.672
		Officer	28 (9.1)	35 (7.6)	1.22 (0.73,2.06)	0.445
		Enlisted Flyer	22 (16.5)	37 (20.0)	0.79 (0.44,1.42)	0.434
		Enlisted Groundcrew	60 (17.8)	86 (16.4)	1.11 (0.77,1.59)	0.587
9-4	Appearance of Illness or Distress	All	31 (4.0)	50 (4.3)	0.94 (0.59,1.48)	0.774
		Officer	12 (3.9)	18 (3.9)	1.01 (0.48,2.12)	0.986
		Enlisted Flyer	11 (8.3)	8 (4.3)	1.99 (0.78,5.10)	0.150
		Enlisted Groundcrew	8 (2.4)	24 (4.6)	0.51 (0.23,1.15)	0.104
9-5	Relative Age Appearance	All	42 (5.4)	48 (4.1)	1.34 (0.88,2.05)	0.176
		Officer	6 (2.0)	7 (1.5)	1.30 (0.43,3.91)	0.640
		Enlisted Flyer	13 (9.8)	17 (9.2)	1.07 (0.50,2.29)	0.860
		Enlisted Groundcrew	23 (6.8)	24 (4.6)	1.54 (0.85,2.77)	0.154
9-7	Body Mass Index	All	274 (35.3)	415 (35.3)	1.00 (0.83,1.21)	0.986
		Officer	93 (30.4)	139 (30.1)	1.01 (0.74,1.39)	0.928
		Enlisted Flyer	48 (36.1)	68 (36.8)	0.97 (0.61,1.54)	0.903
		Enlisted Groundcrew	133 (39.5)	208 (39.5)	1.00 (0.76,1.32)	0.999
10-3	All Skin Neoplasms	All	391 (54.2)	519 (47.8)	1.29 (1.07,1.56)	0.007
		Officer	172 (58.1)	228 (50.9)	1.34 (1.00,1.80)	0.054
		Enlisted Flyer	70 (56.9)	86 (50.6)	1.29 (0.81,2.06)	0.285
		Enlisted Groundcrew	149 (49.3)	205 (43.8)	1.25 (0.93,1.67)	0.133
10-4	Malignant Skin Neoplasms	All	183 (25.4)	234 (21.5)	1.24 (0.99,1.55)	0.059
		Officer	94 (31.8)	114 (25.4)	1.36 (0.99,1.89)	0.061
		Enlisted Flyer	36 (29.3)	38 (22.4)	1.44 (0.85,2.44)	0.180
		Enlisted Groundcrew	53 (17.5)	82 (17.5)	1.00 (0.68,1.47)	0.992
10-5	Benign Skin Neoplasms	All	295 (38.3)	397 (34.2)	1.20 (0.99,1.44)	0.065
		Officer	117 (38.6)	158 (34.7)	1.18 (0.87,1.60)	0.276
		Enlisted Flyer	51 (38.6)	65 (35.5)	1.14 (0.72,1.82)	0.572
		Enlisted Groundcrew	127 (37.9)	174 (33.3)	1.22 (0.92,1.63)	0.165
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	All	8 (1.1)	5 (0.5)	2.43 (0.79,7.44)	0.115
		Officer	5 (1.7)	3 (0.7)	2.55 (0.60,10.75)	0.203
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	3 (1.0)	2 (0.4)	2.34 (0.39,14.07)	0.354
10-7	Basal Cell Carcinoma	All	154 (21.4)	183 (16.9)	1.34 (1.06,1.70)	0.017
		Officer	83 (28.0)	87 (19.4)	1.62 (1.14,2.28)	0.006
		Enlisted Flyer	29 (23.6)	30 (17.6)	1.44 (0.81,2.55)	0.213
		Enlisted Groundcrew	42 (13.9)	66 (14.1)	0.98 (0.65,1.49)	0.939
10-8	Squamous Cell Carcinoma	All	45 (6.2)	61 (5.6)	1.12 (0.75,1.66)	0.581
		Officer	24 (8.1)	36 (8.0)	1.01 (0.59,1.73)	0.972
		Enlisted Flyer	9 (7.3)	8 (4.7)	1.60 (0.60,4.27)	0.349
		Enlisted Groundcrew	12 (4.0)	17 (3.6)	1.10 (0.52,2.33)	0.808

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
10-9	Nonmelanoma	All	17 (24.3)	213 (19.6)	1.31 (1.05,1.65)	0.019
		Officer	91 (30.7)	103 (23.0)	1.49 (1.07,2.07)	0.019
		Enlisted Flyer	36 (29.3)	35 (20.6)	1.60 (0.93,2.73)	0.088
		Enlisted Groundcrew	48 (15.9)	75 (16.0)	0.99 (0.67,1.47)	0.961
10-10	Melanoma	All	19 (2.6)	31 (2.9)	0.92 (0.52,1.64)	0.780
		Officer	11 (3.7)	17 (3.8)	0.98 (0.45,2.12)	0.956
		Enlisted Flyer	1 (0.8)	5 (2.9)	0.27 (0.03,2.34)	0.235
		Enlisted Groundcrew	7 (2.3)	9 (1.9)	1.21 (0.45,3.28)	0.708
10-11	All Systemic Neoplasms	All	262 (34.2)	389 (33.2)	1.05 (0.86,1.27)	0.649
		Officer	115 (38.2)	172 (37.5)	1.03 (0.76,1.39)	0.838
		Enlisted Flyer	48 (37.2)	62 (33.5)	1.18 (0.73,1.88)	0.500
		Enlisted Groundcrew	99 (29.6)	155 (29.5)	1.00 (0.74,1.36)	0.979
10-12	Malignant Systemic Neoplasms	All	97 (12.6)	118 (10.1)	1.29 (0.97,1.72)	0.082
		Officer	50 (16.6)	50 (10.8)	1.63 (1.07,2.49)	0.023
		Enlisted Flyer	25 (19.1)	21 (11.4)	1.84 (0.98,3.46)	0.057
		Enlisted Groundcrew	22 (6.5)	47 (8.9)	0.71 (0.42,1.21)	0.209
10-13	Benign Systemic Neoplasms	All	192 (25.1)	294 (25.1)	1.00 (0.81,1.23)	0.988
		Officer	80 (26.6)	133 (29.0)	0.89 (0.64,1.23)	0.472
		Enlisted Flyer	29 (22.5)	46 (24.9)	0.88 (0.52,1.49)	0.626
		Enlisted Groundcrew	83 (24.8)	115 (21.9)	1.18 (0.85,1.63)	0.322
10-14	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	All	15 (2.0)	25 (2.1)	0.91 (0.48,1.74)	0.781
		Officer	7 (2.3)	13 (2.8)	0.82 (0.32,2.07)	0.672
		Enlisted Flyer	3 (2.3)	2 (1.1)	2.14 (0.35,13.02)	0.407
		Enlisted Groundcrew	5 (1.5)	10 (1.9)	0.78 (0.26,2.30)	0.652
10-16	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	All	1 (0.1)	4 (0.3)	0.38 (0.04,3.41)	0.347
		Officer	0 (0.0)	1 (0.2)	--	0.999[a]
		Enlisted Flyer	1 (0.8)	1 (0.5)	1.42 (0.09,22.84)	0.807
		Enlisted Groundcrew	0 (0.0)	2 (0.4)	--	0.685[a]
10-17	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	All	4 (0.5)	9 (0.8)	0.68 (0.21,2.20)	0.506
		Officer	1 (0.3)	3 (0.7)	0.51 (0.05,4.90)	0.557
		Enlisted Flyer	3 (2.3)	2 (1.1)	2.14 (0.35,13.02)	0.407
		Enlisted Groundcrew	0 (0.0)	4 (0.8)	--	0.276[a]
10-18	Malignant Systemic Neoplasms (Thymus, Heart, & Mediastinum)	All	2 (0.3)	1 (0.1)	3.05 (0.28,33.73)	0.344
		Officer	1 (0.3)	0 (0.0)	--	0.831[a]
		Enlisted Flyer	0 (0.0)	1 (0.5)	--	0.999[a]
		Enlisted Groundcrew	1 (0.3)	0 (0.0)	--	0.821[a]
10-19	Malignant Systemic Neoplasms (Thyroid Gland)	All	1 (0.1)	2 (0.2)	0.76 (0.07,8.42)	0.822
		Officer	1 (0.3)	1 (0.2)	1.53 (0.10,24.53)	0.765
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	0 (0.0)	1 (0.2)	--	0.999[a]

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal				Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand		Comparison			
10-20	Malignant Systemic Neoplasms (Bronchus and Lung)	All	13	(1.7)	7	(0.6)	2.86 (1.14,7.21)	0.021
		Officer	6	(2.0)	3	(0.7)	3.09 (0.77,12.47)	0.112
		Enlisted Flyer	3	(2.3)	3	(1.6)	1.42 (0.28,7.16)	0.669
		Enlisted Groundcrew	4	(1.2)	1	(0.2)	6.33 (0.70,56.84)	0.100
10-21	All Stomach Neoplasms	All	6	(0.8)	8	(0.7)	1.14 (0.40,3.31)	0.804
		Officer	1	(0.3)	5	(1.1)	0.30 (0.04,2.61)	0.277
		Enlisted Flyer	3	(2.3)	1	(0.5)	4.31 (0.44,41.93)	0.208
		Enlisted Groundcrew	2	(0.6)	2	(0.4)	1.57 (0.22,11.19)	0.653
10-22	Malignant Systemic Neoplasms (Colon and Rectum)	All	12	(1.6)	10	(0.9)	1.84 (0.79,4.28)	0.155
		Officer	8	(2.6)	3	(0.7)	4.15 (1.09,15.79)	0.037
		Enlisted Flyer	1	(0.8)	3	(1.6)	0.47 (0.05,4.54)	0.511
		Enlisted Groundcrew	3	(0.9)	4	(0.8)	1.18 (0.26,5.29)	0.833
10-23	Malignant Systemic Neoplasms (Urinary System)	All	18	(2.3)	12	(1.0)	2.32 (1.11,4.84)	0.023
		Officer	8	(2.6)	5	(1.1)	2.48 (0.80,7.66)	0.114
		Enlisted Flyer	4	(3.1)	1	(0.5)	5.80 (0.64,52.46)	0.118
		Enlisted Groundcrew	6	(1.8)	6	(1.1)	1.58 (0.50,4.93)	0.434
10-24	Malignant Systemic Neoplasms (Kidney and Ureter)	All	7	(0.9)	4	(0.3)	2.68 (0.78,9.19)	0.107
		Officer	2	(0.7)	1	(0.2)	3.07 (0.28,33.97)	0.361
		Enlisted Flyer	1	(0.8)	0	(0.0)	--	0.862[a]
		Enlisted Groundcrew	4	(1.2)	3	(0.6)	2.10 (0.47,9.44)	0.333
10-25	Malignant Systemic Neoplasms (Prostate)	All	53	(6.9)	67	(5.7)	1.22 (0.84,1.77)	0.296
		Officer	26	(8.6)	31	(6.7)	1.31 (0.76,2.25)	0.334
		Enlisted Flyer	14	(10.7)	10	(5.4)	2.09 (0.90,4.87)	0.086
		Enlisted Groundcrew	13	(3.9)	26	(4.9)	0.77 (0.39,1.53)	0.460
10-26	Malignant Systemic Neoplasms (Penis and Other Male Genital Organs)	All	2	(0.3)	0	(0.0)	--	0.306[a]
		Officer	0	(0.0)	0	(0.0)	--	--
		Enlisted Flyer	2	(1.5)	0	(0.0)	--	0.334[a]
		Enlisted Groundcrew	0	(0.0)	0	(0.0)	--	--
10-27	Malignant Systemic Neoplasms (Testicles)	All	3	(0.4)	0	(0.0)	--	0.121[a]
		Officer	1	(0.3)	0	(0.0)	--	0.831[a]
		Enlisted Flyer	1	(0.8)	0	(0.0)	--	0.862[a]
		Enlisted Groundcrew	1	(0.3)	0	(0.0)	--	0.821[a]
10-28	Malignant Systemic Neoplasms (Bone and Articular Cartilage)	All	0	(0.0)	4	(0.3)	--	0.267[a]
		Officer	0	(0.0)	1	(0.2)	--	0.999[a]
		Enlisted Flyer	0	(0.0)	2	(1.1)	--	0.636[a]
		Enlisted Groundcrew	0	(0.0)	1	(0.2)	--	0.999[a]
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	All	1	(0.1)	6	(0.5)	0.25 (0.03,2.11)	0.141
		Officer	0	(0.0)	3	(0.7)	--	0.416[a]
		Enlisted Flyer	1	(0.8)	1	(0.5)	1.42 (0.09,22.84)	0.807
		Enlisted Groundcrew	0	(0.0)	2	(0.4)	--	0.685[a]

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
10-30	Carcinoma in Situ	All	4 (0.5)	6 (0.5)	1.02 (0.29,3.61)	0.980
		Officer	2 (0.7)	1 (0.2)	3.07 (0.28,33.97)	0.361
		Enlisted Flyer	2 (1.5)	3 (1.6)	0.94 (0.15,5.71)	0.947
		Enlisted Groundcrew	0 (0.0)	2 (0.4)	--	0.685[a]
10-31	Hodgkin's Disease	All	1 (0.1)	1 (0.1)	1.52 (0.10,24.41)	0.766
		Officer	1 (0.3)	0 (0.0)	--	0.831[a]
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	0 (0.0)	1 (0.2)	--	0.999[a]
10-32	Leukemia	All	4 (0.5)	6 (0.5)	1.02 (0.29,3.61)	0.980
		Officer	3 (1.0)	4 (0.9)	1.15 (0.25,5.16)	0.859
		Enlisted Flyer	1 (0.8)	0 (0.0)	--	0.862[a]
		Enlisted Groundcrew	0 (0.0)	2 (0.4)	--	0.685[a]
10-33	Other Malignant Systemic Neoplasms (Lymphoid and Histiocytic Tissue)	All	6 (0.8)	9 (0.8)	1.02 (0.36,2.87)	0.976
		Officer	3 (1.0)	2 (0.4)	2.30 (0.38,13.86)	0.362
		Enlisted Flyer	1 (0.8)	4 (2.2)	0.35 (0.04,3.15)	0.348
		Enlisted Groundcrew	2 (0.6)	3 (0.6)	1.04 (0.17,6.28)	0.963
10-34	Lymphoreticular Sarcoma	All	1 (0.1)	3 (0.3)	0.51 (0.05,4.89)	0.537
		Officer	1 (0.3)	3 (0.7)	0.51 (0.05,4.90)	0.557
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	0 (0.0)	0 (0.0)	--	--
10-35	Skin and Systemic Neoplasms	All	503 (66.3)	714 (61.7)	1.21 (1.01,1.48)	0.042
		Officer	213 (71.5)	300 (66.4)	1.27 (0.92,1.75)	0.159
		Enlisted Flyer	91 (71.1)	120 (65.6)	1.29 (0.79,2.11)	0.306
		Enlisted Groundcrew	199 (59.8)	294 (56.3)	1.15 (0.87,1.52)	0.321
10-36	Malignant Skin and Systemic Neoplasms	All	241 (31.6)	318 (27.4)	1.22 (1.00,1.49)	0.049
		Officer	120 (40.3)	147 (32.4)	1.41 (1.04,1.91)	0.027
		Enlisted Flyer	51 (39.2)	53 (29.0)	1.58 (0.98,2.55)	0.058
		Enlisted Groundcrew	70 (21.0)	118 (22.6)	0.91 (0.65,1.27)	0.570
10-38	PSA	All	32 (4.5)	58 (5.3)	0.83 (0.54,1.30)	0.418
		Officer	18 (6.6)	29 (6.9)	0.94 (0.51,1.73)	0.851
		Enlisted Flyer	5 (4.3)	10 (5.8)	0.72 (0.24,2.16)	0.556
		Enlisted Groundcrew	9 (2.8)	19 (3.8)	0.73 (0.32,1.62)	0.435
11-3	Inflammatory Diseases	All	9 (1.2)	7 (0.6)	1.94 (0.72,5.23)	0.188
		Officer	3 (1.0)	1 (0.2)	4.50 (0.47,43.46)	0.194
		Enlisted Flyer	2 (1.5)	1 (0.6)	2.75 (0.25,30.63)	0.411
		Enlisted Groundcrew	4 (1.2)	5 (1.0)	1.26 (0.33,4.71)	0.736
11-4	Hereditary and Degenerative Diseases	All	128 (16.5)	163 (13.9)	1.22 (0.95,1.57)	0.118
		Officer	57 (18.6)	57 (12.4)	1.62 (1.08,2.41)	0.019
		Enlisted Flyer	27 (20.3)	28 (15.3)	1.41 (0.79,2.53)	0.248
		Enlisted Groundcrew	44 (13.2)	78 (14.9)	0.87 (0.58,1.29)	0.491

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
11-5	Peripheral Disorders	All	211 (27.4)	305 (26.2)	1.06 (0.87,1.31)	0.556
		Officer	90 (29.4)	117 (25.5)	1.22 (0.88,1.68)	0.232
		Enlisted Flyer	38 (28.8)	52 (28.6)	1.01 (0.62,1.66)	0.967
		Enlisted Groundcrew	83 (24.9)	136 (25.9)	0.95 (0.69,1.30)	0.748
11-6	Other Neurological Disorders	All	152 (19.7)	198 (17.0)	1.20 (0.95,1.51)	0.131
		Officer	24 (7.8)	40 (8.7)	0.89 (0.53,1.52)	0.676
		Enlisted Flyer	44 (33.1)	43 (23.6)	1.60 (0.97,2.63)	0.065
		Enlisted Groundcrew	84 (25.2)	115 (21.9)	1.20 (0.87,1.66)	0.268
11-7	Smell	All	21 (2.7)	27 (2.3)	1.18 (0.66,2.10)	0.576
		Officer	8 (2.6)	13 (2.8)	0.93 (0.38,2.26)	0.864
		Enlisted Flyer	3 (2.3)	5 (2.7)	0.82 (0.19,3.48)	0.784
		Enlisted Groundcrew	10 (3.0)	9 (1.7)	1.77 (0.71,4.40)	0.220
11-8	Visual Fields	All	12 (1.6)	7 (0.6)	2.60 (1.02,6.64)	0.040
		Officer	6 (2.0)	2 (0.4)	4.62 (0.93,23.02)	0.062
		Enlisted Flyer	3 (2.3)	1 (0.6)	4.15 (0.43,40.39)	0.220
		Enlisted Groundcrew	3 (0.9)	4 (0.8)	1.17 (0.26,5.24)	0.841
11-9	Light Reaction	All	4 (0.5)	8 (0.7)	0.75 (0.23,2.51)	0.640
		Officer	1 (0.3)	2 (0.4)	0.75 (0.07,8.33)	0.817
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	3 (0.9)	6 (1.1)	0.78 (0.19,3.14)	0.726
11-10	Ocular Movement	All	5 (0.6)	4 (0.3)	1.89 (0.51,7.07)	0.341
		Officer	2 (0.7)	2 (0.4)	1.51 (0.21,10.78)	0.681
		Enlisted Flyer	1 (0.8)	0 (0.0)	--	0.872[a]
		Enlisted Groundcrew	2 (0.6)	2 (0.4)	1.57 (0.22,11.19)	0.653
11-11	Facial Sensation	All	4 (0.5)	3 (0.3)	2.02 (0.45,9.06)	0.354
		Officer	1 (0.3)	1 (0.2)	1.51 (0.09,24.20)	0.772
		Enlisted Flyer	1 (0.8)	2 (1.1)	0.69 (0.06,7.64)	0.759
		Enlisted Groundcrew	2 (0.6)	0 (0.0)	--	0.294[a]
11-12	Corneal Reflex	All	2 (0.3)	5 (0.4)	0.60 (0.12,3.11)	0.530
		Officer	1 (0.3)	2 (0.4)	0.75 (0.07,8.33)	0.817
		Enlisted Flyer	0 (0.0)	1 (0.6)	--	0.999[a]
		Enlisted Groundcrew	1 (0.3)	2 (0.4)	0.78 (0.07,8.64)	0.840
11-13	Smile	All	8 (1.0)	11 (0.9)	1.10 (0.44,2.75)	0.837
		Officer	4 (1.3)	6 (1.3)	1.00 (0.28,3.59)	0.995
		Enlisted Flyer	1 (0.8)	2 (1.1)	0.69 (0.06,7.64)	0.759
		Enlisted Groundcrew	3 (0.9)	3 (0.6)	1.58 (0.32,7.86)	0.578
11-14	Palpebral Fissure	All	23 (3.0)	23 (2.0)	1.53 (0.85,2.74)	0.158
		Officer	9 (2.9)	10 (2.2)	1.37 (0.55,3.40)	0.502
		Enlisted Flyer	5 (3.8)	6 (3.3)	1.15 (0.34,3.86)	0.818
		Enlisted Groundcrew	9 (2.7)	7 (1.3)	2.05 (0.75,5.55)	0.160

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal				Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand		Comparison			
11-15	Balance	All	18	(2.3)	22	(1.9)	1.24 (0.66,2.33)	0.499
		Officer	10	(3.3)	9	(2.0)	1.70 (0.68,4.23)	0.256
		Enlisted Flyer	5	(3.8)	5	(2.7)	1.39 (0.39,4.90)	0.608
		Enlisted Groundcrew	3	(0.9)	8	(1.5)	0.59 (0.15,2.23)	0.433
11-16	Gag Reflex	All	2	(0.3)	1	(0.1)	3.03 (0.27,33.47)	0.348
		Officer	0	(0.0)	0	(0.0)	--	--
		Enlisted Flyer	1	(0.8)	1	(0.5)	1.38 (0.09,22.24)	0.821
		Enlisted Groundcrew	1	(0.3)	0	(0.0)	--	0.820[a]
11-17	Speech	All	10	(1.3)	12	(1.0)	1.26 (0.54,2.94)	0.589
		Officer	4	(1.3)	4	(0.9)	1.51 (0.38,6.10)	0.560
		Enlisted Flyer	1	(0.8)	1	(0.5)	1.38 (0.09,22.24)	0.821
		Enlisted Groundcrew	5	(1.5)	7	(1.3)	1.12 (0.35,3.57)	0.842
11-18	Tongue Position Relative to Midline	All	3	(0.4)	2	(0.2)	2.27 (0.38,13.64)	0.362
		Officer	1	(0.3)	1	(0.2)	1.51 (0.09,24.20)	0.772
		Enlisted Flyer	1	(0.8)	1	(0.5)	1.38 (0.09,22.24)	0.821
		Enlisted Groundcrew	1	(0.3)	0	(0.0)	--	0.820[a]
11-19	Shoulder Shrug	All	3	(0.4)	6	(0.5)	0.76 (0.19,3.03)	0.688
		Officer	2	(0.7)	2	(0.4)	1.51 (0.21,10.78)	0.681
		Enlisted Flyer	0	(0.0)	2	(1.1)	--	0.623[a]
		Enlisted Groundcrew	1	(0.3)	2	(0.4)	0.79 (0.07,8.69)	0.844
11-20	Cranial Nerve Index	All	82	(10.7)	89	(7.7)	1.43 (1.05,1.97)	0.025
		Officer	35	(11.6)	36	(7.8)	1.54 (0.94,2.51)	0.085
		Enlisted Flyer	15	(11.3)	16	(8.8)	1.32 (0.63,2.77)	0.465
		Enlisted Groundcrew	32	(9.6)	37	(7.2)	1.38 (0.84,2.26)	0.204
11-21	Pinprick	All	69	(10.8)	88	(8.9)	1.24 (0.89,1.72)	0.212
		Officer	26	(10.1)	32	(8.2)	1.25 (0.73,2.16)	0.415
		Enlisted Flyer	14	(13.7)	20	(13.0)	1.07 (0.51,2.22)	0.865
		Enlisted Groundcrew	29	(10.5)	36	(8.2)	1.31 (0.78,2.19)	0.300
11-22	Light Touch	All	40	(6.3)	56	(5.7)	1.11 (0.73,1.69)	0.625
		Officer	16	(6.2)	17	(4.4)	1.45 (0.72,2.93)	0.299
		Enlisted Flyer	7	(6.9)	14	(9.1)	0.74 (0.29,1.89)	0.526
		Enlisted Groundcrew	17	(6.1)	25	(5.7)	1.09 (0.57,2.05)	0.800
11-23	Muscle Status	All	43	(5.6)	58	(5.0)	1.14 (0.76,1.70)	0.541
		Officer	17	(5.6)	21	(4.6)	1.25 (0.65,2.40)	0.512
		Enlisted Flyer	8	(6.0)	12	(6.6)	0.91 (0.36,2.30)	0.845
		Enlisted Groundcrew	18	(5.4)	25	(4.8)	1.14 (0.61,2.13)	0.671
11-27	Babinski Reflex	All	10	(1.3)	18	(1.5)	0.84 (0.38,1.82)	0.650
		Officer	3	(1.0)	4	(0.9)	1.13 (0.25,5.07)	0.877
		Enlisted Flyer	4	(3.0)	4	(2.2)	1.39 (0.34,5.65)	0.648
		Enlisted Groundcrew	3	(0.9)	10	(1.9)	0.47 (0.13,1.71)	0.249

**Table G-5. Summary of Unadjusted Results for Dichotomous Variables – Model 1
(Ranch Hands vs. Comparisons) (Continued)**

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
11-28	Any Symmetric Peripheral Abnormality	All	185 (24.7)	249 (22.0)	1.16 (0.93,1.44)	0.186
		Officer	77 (25.8)	101 (22.7)	1.19 (0.84,1.67)	0.326
		Enlisted Flyer	39 (30.0)	44 (25.0)	1.29 (0.77,2.13)	0.331
		Enlisted Groundcrew	69 (21.4)	104 (20.4)	1.06 (0.75,1.50)	0.730
11-29	Possible Peripheral Neuropathy	All	175 (23.3)	242 (21.4)	1.12 (0.90,1.39)	0.323
		Officer	72 (24.2)	99 (22.2)	1.11 (0.79,1.57)	0.544
		Enlisted Flyer	37 (28.5)	42 (23.7)	1.28 (0.76,2.14)	0.349
		Enlisted Groundcrew	66 (20.5)	101 (19.8)	1.04 (0.74,1.47)	0.819
11-30	Probable Peripheral Neuropathy	All	62 (8.3)	79 (7.0)	1.20 (0.85,1.70)	0.300
		Officer	31 (10.4)	33 (7.4)	1.45 (0.87,2.42)	0.157
		Enlisted Flyer	14 (10.8)	14 (7.9)	1.41 (0.65,3.06)	0.392
		Enlisted Groundcrew	17 (5.3)	32 (6.3)	0.83 (0.45,1.53)	0.556
11-31	Tremor	All	54 (7.0)	86 (7.4)	0.95 (0.66,1.35)	0.757
		Officer	20 (6.5)	32 (6.9)	0.94 (0.53,1.67)	0.827
		Enlisted Flyer	10 (7.5)	14 (7.7)	0.98 (0.42,2.28)	0.965
		Enlisted Groundcrew	24 (7.2)	40 (7.6)	0.94 (0.55,1.59)	0.814
11-32	Coordination	All	31 (4.0)	61 (5.2)	0.76 (0.49,1.18)	0.221
		Officer	13 (4.2)	19 (4.1)	1.03 (0.50,2.12)	0.931
		Enlisted Flyer	6 (4.5)	13 (7.1)	0.62 (0.23,1.68)	0.351
		Enlisted Groundcrew	12 (3.6)	29 (5.5)	0.64 (0.32,1.27)	0.203
11-33	Romberg Sign	All	18 (2.3)	22 (1.9)	1.24 (0.66,2.33)	0.499
		Officer	10 (3.3)	9 (2.0)	1.70 (0.68,4.23)	0.256
		Enlisted Flyer	5 (3.8)	5 (2.7)	1.39 (0.39,4.90)	0.608
		Enlisted Groundcrew	3 (0.9)	8 (1.5)	0.59 (0.15,2.23)	0.433
11-34	Gait	All	65 (8.4)	98 (8.4)	1.00 (0.72,1.39)	0.984
		Officer	27 (8.8)	36 (7.8)	1.14 (0.68,1.92)	0.617
		Enlisted Flyer	12 (9.0)	20 (10.9)	0.81 (0.38,1.72)	0.580
		Enlisted Groundcrew	26 (7.8)	42 (8.0)	0.97 (0.58,1.62)	0.909
11-35	CNS Index	All	113 (14.6)	183 (15.7)	0.92 (0.72,1.19)	0.533
		Officer	45 (14.7)	64 (13.9)	1.07 (0.71,1.61)	0.749
		Enlisted Flyer	21 (15.8)	34 (18.6)	0.82 (0.45,1.49)	0.519
		Enlisted Groundcrew	47 (14.1)	85 (16.2)	0.85 (0.58,1.25)	0.402
12-3	Psychoses	All	46 (5.9)	74 (6.3)	0.94 (0.64,1.37)	0.739
		Officer	8 (2.6)	15 (3.3)	0.80 (0.33,1.90)	0.607
		Enlisted Flyer	13 (9.8)	12 (6.5)	1.56 (0.69,3.54)	0.286
		Enlisted Groundcrew	25 (7.5)	47 (8.9)	0.82 (0.50,1.37)	0.455
12-4	Alcohol Dependence	All	46 (5.9)	66 (5.6)	1.06 (0.72,1.56)	0.776
		Officer	10 (3.3)	21 (4.6)	0.71 (0.33,1.52)	0.373
		Enlisted Flyer	8 (6.0)	13 (7.0)	0.85 (0.34,2.10)	0.720
		Enlisted Groundcrew	28 (8.4)	32 (6.1)	1.41 (0.83,2.39)	0.201

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
12-5	Drug Dependence	All	2 (0.3)	5 (0.4)	0.60 (0.12,3.12)	0.535
		Officer	0 (0.0)	1 (0.2)	--	0.999[a]
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	2 (0.6)	4 (0.8)	0.79 (0.14,4.32)	0.782
12-6	Anxiety	All	226 (29.3)	331 (28.3)	1.05 (0.86,1.28)	0.635
		Officer	50 (16.3)	90 (19.5)	0.80 (0.55,1.17)	0.256
		Enlisted Flyer	44 (33.3)	59 (31.9)	1.07 (0.66,1.72)	0.787
		Enlisted Groundcrew	132 (39.8)	182 (34.8)	1.24 (0.93,1.64)	0.143
12-7	Other Neuroses	All	454 (59.3)	692 (59.6)	0.99 (0.82,1.19)	0.901
		Officer	133 (43.5)	236 (51.5)	0.72 (0.54,0.97)	0.029
		Enlisted Flyer	92 (69.7)	122 (66.7)	1.15 (0.71,1.86)	0.570
		Enlisted Groundcrew	229 (69.8)	334 (64.1)	1.30 (0.96,1.74)	0.087
12-8	SCL-90-R Anxiety	All	65 (8.4)	106 (9.1)	0.92 (0.67,1.28)	0.629
		Officer	8 (2.6)	21 (4.6)	0.56 (0.25,1.28)	0.170
		Enlisted Flyer	12 (9.0)	20 (10.8)	0.82 (0.39,1.74)	0.602
		Enlisted Groundcrew	45 (13.6)	65 (12.4)	1.11 (0.74,1.67)	0.617
12-9	SCL-90-R Depression	All	85 (11.0)	143 (12.2)	0.89 (0.67,1.18)	0.419
		Officer	19 (6.2)	38 (8.2)	0.73 (0.42,1.30)	0.289
		Enlisted Flyer	13 (9.8)	22 (11.9)	0.80 (0.39,1.66)	0.552
		Enlisted Groundcrew	53 (16.0)	83 (15.8)	1.01 (0.69,1.47)	0.952
12-10	SCL-90-R Hostility	All	41 (5.3)	65 (5.6)	0.95 (0.64,1.43)	0.819
		Officer	4 (1.3)	12 (2.6)	0.49 (0.16,1.55)	0.226
		Enlisted Flyer	8 (6.0)	16 (8.6)	0.68 (0.28,1.63)	0.383
		Enlisted Groundcrew	29 (8.7)	37 (7.0)	1.26 (0.76,2.10)	0.368
12-11	SCL-90-R Interpersonal Sensitivity	All	57 (7.4)	125 (10.7)	0.67 (0.48,0.93)	0.014
		Officer	10 (3.3)	31 (6.7)	0.47 (0.23,0.97)	0.040
		Enlisted Flyer	12 (9.0)	25 (13.5)	0.63 (0.31,1.31)	0.221
		Enlisted Groundcrew	35 (10.5)	69 (13.1)	0.78 (0.51,1.20)	0.257
12-12	SCL-90-R Obsessive-compulsive Behavior	All	125 (16.2)	212 (18.1)	0.87 (0.69,1.11)	0.274
		Officer	31 (10.1)	55 (11.9)	0.83 (0.52,1.32)	0.431
		Enlisted Flyer	24 (18.0)	38 (20.5)	0.85 (0.48,1.50)	0.580
		Enlisted Groundcrew	70 (21.1)	119 (22.7)	0.91 (0.65,1.27)	0.586
12-13	SCL-90-R Paranoid Ideation	All	24 (3.1)	65 (5.6)	0.55 (0.34,0.88)	0.010
		Officer	3 (1.0)	11 (2.4)	0.40 (0.11,1.46)	0.166
		Enlisted Flyer	5 (3.8)	8 (4.3)	0.86 (0.28,2.70)	0.802
		Enlisted Groundcrew	16 (4.8)	46 (8.8)	0.53 (0.29,0.95)	0.032
12-14	SCL-90-R Phobic Anxiety	All	55 (7.1)	100 (8.5)	0.82 (0.58,1.16)	0.257
		Officer	5 (1.6)	17 (3.7)	0.43 (0.16,1.18)	0.103
		Enlisted Flyer	13 (9.8)	21 (11.4)	0.85 (0.41,1.76)	0.654
		Enlisted Groundcrew	37 (11.1)	62 (11.8)	0.94 (0.61,1.44)	0.767

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
12-15	SCL-90-R Psychoticism	All	69 (8.9)	123 (10.5)	0.84 (0.61,1.14)	0.255
		Officer	18 (5.9)	30 (6.5)	0.89 (0.49,1.64)	0.718
		Enlisted Flyer	12 (9.0)	21 (11.4)	0.77 (0.37,1.63)	0.503
		Enlisted Groundcrew	39 (11.7)	72 (13.7)	0.84 (0.55,1.27)	0.404
12-16	SCL-90-R Somatization	All	104 (13.5)	172 (14.7)	0.90 (0.70,1.18)	0.451
		Officer	21 (6.8)	35 (7.6)	0.89 (0.51,1.57)	0.695
		Enlisted Flyer	26 (19.5)	34 (18.4)	1.08 (0.61,1.90)	0.792
		Enlisted Groundcrew	57 (17.2)	103 (19.6)	0.85 (0.59,1.21)	0.370
12-17	SCL-90-R Global Severity Index	All	81 (10.5)	143 (12.2)	0.84 (0.63,1.13)	0.243
		Officer	14 (4.6)	30 (6.5)	0.69 (0.36,1.32)	0.258
		Enlisted Flyer	12 (9.0)	24 (13.0)	0.67 (0.32,1.38)	0.275
		Enlisted Groundcrew	55 (16.6)	89 (17.0)	0.97 (0.67,1.41)	0.883
12-18	SCL-90-R Positive Symptom Total	All	74 (9.6)	147 (12.6)	0.74 (0.55,0.99)	0.042
		Officer	16 (5.2)	37 (8.0)	0.63 (0.34,1.15)	0.135
		Enlisted Flyer	11 (8.3)	22 (11.9)	0.67 (0.31,1.43)	0.299
		Enlisted Groundcrew	47 (14.2)	88 (16.8)	0.82 (0.56,1.20)	0.308
12-19	SCL-90-R Positive Symptom Distress Index	All	55 (7.1)	96 (8.2)	0.86 (0.61,1.21)	0.385
		Officer	10 (3.3)	13 (2.8)	1.16 (0.50,2.68)	0.728
		Enlisted Flyer	10 (7.5)	28 (15.1)	0.46 (0.21,0.97)	0.043
		Enlisted Groundcrew	35 (10.5)	55 (10.5)	1.01 (0.64,1.58)	0.976
13-3	Uncharacterized Hepatitis	All	15 (1.9)	15 (1.3)	1.53 (0.74,3.14)	0.253
		Officer	3 (1.0)	6 (1.3)	0.75 (0.19,3.01)	0.681
		Enlisted Flyer	3 (2.3)	1 (0.5)	4.25 (0.44,41.28)	0.213
		Enlisted Groundcrew	9 (2.7)	8 (1.5)	1.80 (0.69,4.71)	0.232
13-4	Jaundice	All	14 (1.9)	33 (2.9)	0.64 (0.34,1.20)	0.150
		Officer	7 (2.4)	16 (3.6)	0.65 (0.27,1.61)	0.354
		Enlisted Flyer	2 (1.5)	1 (0.6)	2.76 (0.25,30.76)	0.409
		Enlisted Groundcrew	5 (1.5)	16 (3.1)	0.49 (0.18,1.34)	0.163
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	All	33 (4.5)	45 (4.0)	1.13 (0.71,1.78)	0.614
		Officer	12 (4.1)	11 (2.5)	1.65 (0.72,3.79)	0.237
		Enlisted Flyer	5 (4.2)	6 (3.4)	1.25 (0.37,4.18)	0.721
		Enlisted Groundcrew	16 (5.1)	28 (5.7)	0.90 (0.48,1.69)	0.738
13-6	Chronic Liver Disease and Cirrhosis (Nonalcohol-related)	All	27 (3.5)	27 (2.3)	1.53 (0.89,2.63)	0.125
		Officer	11 (3.6)	8 (1.7)	2.11 (0.84,5.30)	0.113
		Enlisted Flyer	1 (0.8)	7 (3.8)	0.19 (0.02,1.58)	0.126
		Enlisted Groundcrew	15 (4.5)	12 (2.3)	2.00 (0.92,4.33)	0.079
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	All	5 (0.6)	2 (0.2)	3.80 (0.73,19.61)	0.090
		Officer	2 (0.7)	1 (0.2)	3.02 (0.27,33.48)	0.367
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	3 (0.9)	1 (0.2)	4.72 (0.49,45.61)	0.180

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
13-8	Enlarged Liver	All	27 (3.5)	45 (3.8)	0.90 (0.56,1.47)	0.682
		Officer	11 (3.6)	14 (3.0)	1.19 (0.53,2.65)	0.676
		Enlisted Flyer	5 (3.8)	6 (3.2)	1.17 (0.35,3.90)	0.804
		Enlisted Groundcrew	11 (3.3)	25 (4.7)	0.68 (0.33,1.40)	0.295
13-9	Other Disorders of the Liver	All	365 (47.2)	527 (45.2)	1.08 (0.90,1.30)	0.406
		Officer	134 (43.9)	199 (43.6)	1.01 (0.76,1.36)	0.936
		Enlisted Flyer	68 (51.1)	88 (47.6)	1.15 (0.74,1.80)	0.531
		Enlisted Groundcrew	163 (48.5)	240 (45.8)	1.11 (0.85,1.47)	0.437
13-10	Current Hepatomegaly	All	12 (1.6)	13 (1.1)	1.39 (0.63,3.06)	0.415
		Officer	6 (2.0)	4 (0.9)	2.29 (0.64,8.17)	0.203
		Enlisted Flyer	0 (0.0)	4 (2.2)	--	0.224[a]
		Enlisted Groundcrew	6 (1.8)	5 (1.0)	1.87 (0.57,6.19)	0.303
13-12	AST	All	65 (8.5)	83 (7.2)	1.19 (0.85,1.67)	0.308
		Officer	29 (9.5)	30 (6.5)	1.50 (0.88,2.56)	0.134
		Enlisted Flyer	10 (7.5)	11 (6.1)	1.26 (0.52,3.05)	0.614
		Enlisted Groundcrew	26 (7.9)	42 (8.2)	0.96 (0.58,1.60)	0.879
13-14	ALT	All	54 (7.0)	88 (7.6)	0.92 (0.64,1.30)	0.625
		Officer	21 (6.9)	25 (5.4)	1.28 (0.71,2.34)	0.414
		Enlisted Flyer	10 (7.5)	17 (9.4)	0.78 (0.35,1.77)	0.559
		Enlisted Groundcrew	23 (7.0)	46 (8.9)	0.76 (0.45,1.28)	0.307
13-16	GGT	All	77 (10.0)	127 (11.0)	0.90 (0.67,1.22)	0.494
		Officer	30 (9.8)	43 (9.4)	1.06 (0.65,1.72)	0.829
		Enlisted Flyer	13 (9.8)	23 (12.7)	0.74 (0.36,1.53)	0.421
		Enlisted Groundcrew	34 (10.3)	61 (11.9)	0.85 (0.55,1.33)	0.483
13-18	Alkaline Phosphatase	All	63 (8.2)	70 (6.1)	1.38 (0.97,1.97)	0.073
		Officer	14 (4.6)	20 (4.4)	1.06 (0.52,2.12)	0.879
		Enlisted Flyer	14 (10.5)	17 (9.4)	1.13 (0.54,2.39)	0.739
		Enlisted Groundcrew	35 (10.6)	33 (6.4)	1.73 (1.05,2.84)	0.031
13-20	Total Bilirubin	All	50 (6.5)	76 (6.6)	0.99 (0.68,1.43)	0.948
		Officer	22 (7.2)	32 (7.0)	1.04 (0.59,1.82)	0.899
		Enlisted Flyer	9 (6.8)	8 (4.4)	1.57 (0.59,4.18)	0.367
		Enlisted Groundcrew	19 (5.8)	36 (7.0)	0.81 (0.46,1.44)	0.475
13-21	Direct Bilirubin	All	2 (0.3)	11 (1.0)	0.27 (0.06,1.23)	0.053
		Officer	2 (0.7)	5 (1.1)	0.60 (0.12,3.11)	0.542
		Enlisted Flyer	0 (0.0)	0 (0.0)	--	--
		Enlisted Groundcrew	0 (0.0)	6 (1.2)	--	0.121[a]
13-23	LDH	All	85 (11.1)	108 (9.4)	1.21 (0.89,1.63)	0.224
		Officer	39 (12.8)	42 (9.2)	1.46 (0.92,2.31)	0.111
		Enlisted Flyer	17 (12.8)	16 (8.8)	1.51 (0.73,3.11)	0.263
		Enlisted Groundcrew	29 (8.8)	50 (9.7)	0.89 (0.55,1.44)	0.648

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
13-25	Cholesterol	All	83 (10.8)	154 (13.3)	0.79 (0.59,1.05)	0.095
		Officer	23 (7.5)	45 (9.8)	0.75 (0.44,1.27)	0.283
		Enlisted Flyer	18 (13.5)	24 (13.3)	1.02 (0.53,1.97)	0.944
		Enlisted Groundcrew	42 (12.7)	85 (16.5)	0.74 (0.49,1.10)	0.132
13-27	HDL Cholesterol	All	139 (18.1)	173 (15.0)	1.25 (0.98,1.60)	0.072
		Officer	47 (15.4)	50 (10.9)	1.49 (0.97,2.29)	0.068
		Enlisted Flyer	23 (17.3)	32 (17.7)	0.97 (0.54,1.76)	0.929
		Enlisted Groundcrew	69 (20.9)	91 (17.7)	1.23 (0.87,1.74)	0.247
13-29	Cholesterol-HDL Ratio	All	241 (31.4)	375 (32.5)	0.95 (0.78,1.16)	0.608
		Officer	67 (22.0)	112 (24.4)	0.87 (0.62,1.23)	0.437
		Enlisted Flyer	42 (31.6)	67 (37.0)	0.79 (0.49,1.26)	0.318
		Enlisted Groundcrew	132 (40.0)	196 (38.1)	1.08 (0.81,1.44)	0.587
13-31	Triglycerides	All	103 (13.4)	113 (9.8)	1.43 (1.07,1.90)	0.015
		Officer	26 (8.5)	33 (7.2)	1.20 (0.70,2.06)	0.499
		Enlisted Flyer	18 (13.5)	19 (10.5)	1.33 (0.67,2.65)	0.411
		Enlisted Groundcrew	59 (17.9)	61 (11.9)	1.62 (1.10,2.38)	0.015
13-33	Creatine Phosphokinase	All	68 (8.9)	124 (10.7)	0.81 (0.59,1.10)	0.173
		Officer	24 (7.9)	38 (8.3)	0.95 (0.56,1.61)	0.839
		Enlisted Flyer	12 (9.0)	23 (12.7)	0.68 (0.33,1.42)	0.307
		Enlisted Groundcrew	32 (9.7)	63 (12.3)	0.77 (0.49,1.21)	0.252
13-35	Serum Amylase	All	22 (2.9)	38 (3.3)	0.87 (0.51,1.48)	0.595
		Officer	3 (1.0)	16 (3.5)	0.28 (0.08,0.95)	0.042
		Enlisted Flyer	5 (3.8)	6 (3.3)	1.14 (0.34,3.82)	0.832
		Enlisted Groundcrew	14 (4.2)	16 (3.1)	1.38 (0.66,2.86)	0.389
13-36	Antibodies for Hepatitis A	All	247 (31.9)	411 (35.0)	0.87 (0.72,1.05)	0.153
		Officer	80 (26.3)	134 (29.0)	0.87 (0.63,1.21)	0.417
		Enlisted Flyer	63 (47.4)	84 (45.4)	1.08 (0.69,1.69)	0.729
		Enlisted Groundcrew	104 (30.9)	193 (36.7)	0.77 (0.58,1.03)	0.079
13-37	Serological Evidence of Prior Hepatitis B Infection	All	50 (6.4)	129 (11.0)	0.56 (0.40,0.78)	<0.001
		Officer	7 (2.3)	25 (5.4)	0.41 (0.17,0.96)	0.039
		Enlisted Flyer	15 (11.3)	32 (17.3)	0.61 (0.31,1.17)	0.138
		Enlisted Groundcrew	28 (8.3)	72 (13.7)	0.57 (0.36,0.91)	0.017
13-38	Antibodies for Hepatitis C	All	5 (0.6)	19 (1.6)	0.39 (0.15,1.06)	0.046
		Officer	1 (0.3)	2 (0.4)	0.75 (0.07,8.33)	0.816
		Enlisted Flyer	0 (0.0)	4 (2.2)	--	0.232[a]
		Enlisted Groundcrew	4 (1.2)	13 (2.5)	0.47 (0.15,1.47)	0.196
13-39	Stool Hemoccult	All	12 (1.7)	15 (1.4)	1.20 (0.56,2.57)	0.645
		Officer	6 (2.1)	1 (0.2)	9.12 (1.09,76.14)	0.041
		Enlisted Flyer	3 (2.4)	2 (1.2)	2.08 (0.34,12.62)	0.427
		Enlisted Groundcrew	3 (1.0)	12 (2.5)	0.38 (0.11,1.36)	0.137

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal				Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand		Comparison			
13-41	Prealbumin	All	16	(2.1)	15	(1.3)	1.62 (0.79,3.29)	0.187
		Officer	7	(2.3)	6	(1.3)	1.77 (0.59,5.33)	0.307
		Enlisted Flyer	1	(0.8)	3	(1.7)	0.45 (0.05,4.37)	0.491
		Enlisted Groundcrew	8	(2.4)	6	(1.2)	2.10 (0.72,6.12)	0.172
13-43	Albumin	All	5	(0.7)	6	(0.5)	1.25 (0.38,4.12)	0.711
		Officer	3	(1.0)	2	(0.4)	2.27 (0.38,13.67)	0.371
		Enlisted Flyer	1	(0.8)	1	(0.6)	1.36 (0.08,22.00)	0.827
		Enlisted Groundcrew	1	(0.3)	3	(0.6)	0.52 (0.05,5.00)	0.569
13-45	α-1-Acid Glycoprotein	All	46	(6.0)	55	(4.8)	1.27 (0.85,1.90)	0.242
		Officer	11	(3.6)	20	(4.4)	0.82 (0.39,1.74)	0.607
		Enlisted Flyer	11	(8.3)	7	(3.9)	2.24 (0.84,5.94)	0.105
		Enlisted Groundcrew	24	(7.3)	28	(5.4)	1.36 (0.77,2.39)	0.283
13-49	α-2-Macroglobulin	All	105	(13.7)	163	(14.1)	0.96 (0.74,1.25)	0.779
		Officer	44	(14.4)	57	(12.4)	1.19 (0.78,1.82)	0.423
		Enlisted Flyer	21	(15.8)	32	(17.7)	0.87 (0.48,1.59)	0.659
		Enlisted Groundcrew	40	(12.1)	74	(14.4)	0.82 (0.54,1.24)	0.346
13-51	Apolipoprotein B	All	9	(1.2)	26	(2.3)	0.51 (0.24,1.10)	0.074
		Officer	4	(1.3)	10	(2.2)	0.60 (0.19,1.92)	0.386
		Enlisted Flyer	1	(0.8)	5	(2.8)	0.27 (0.03,2.31)	0.230
		Enlisted Groundcrew	4	(1.2)	11	(2.1)	0.56 (0.18,1.78)	0.326
13-53	C3 Complement	All	10	(1.3)	21	(1.8)	0.71 (0.33,1.52)	0.371
		Officer	8	(2.6)	12	(2.6)	1.00 (0.41,2.48)	0.994
		Enlisted Flyer	1	(0.8)	5	(2.8)	0.27 (0.03,2.31)	0.230
		Enlisted Groundcrew	1	(0.3)	4	(0.8)	0.39 (0.04,3.48)	0.397
13-55	C4 Complement	All	57	(7.4)	91	(7.9)	0.94 (0.66,1.32)	0.708
		Officer	28	(9.2)	36	(7.8)	1.19 (0.71,1.99)	0.514
		Enlisted Flyer	11	(8.3)	19	(10.5)	0.77 (0.35,1.68)	0.508
		Enlisted Groundcrew	18	(5.5)	36	(7.0)	0.77 (0.43,1.37)	0.371
13-57	Haptoglobin	All	107	(13.9)	134	(11.6)	1.23 (0.94,1.62)	0.134
		Officer	30	(9.8)	39	(8.5)	1.17 (0.71,1.94)	0.527
		Enlisted Flyer	28	(21.1)	25	(13.8)	1.66 (0.92,3.01)	0.093
		Enlisted Groundcrew	49	(14.8)	70	(13.6)	1.11 (0.75,1.64)	0.616
13-59	Transferrin	All	42	(5.5)	72	(6.2)	0.87 (0.59,1.29)	0.482
		Officer	21	(6.9)	33	(7.2)	0.95 (0.54,1.68)	0.872
		Enlisted Flyer	6	(4.5)	16	(8.8)	0.49 (0.19,1.28)	0.145
		Enlisted Groundcrew	15	(4.5)	23	(4.5)	1.02 (0.52,1.98)	0.961
13-61	Prothrombin Time	All	5	(0.9)	8	(0.9)	0.98 (0.32,3.00)	0.967
		Officer	2	(0.9)	3	(0.9)	1.04 (0.17,6.29)	0.964
		Enlisted Flyer	2	(2.2)	3	(2.2)	0.99 (0.16,6.04)	0.990
		Enlisted Groundcrew	1	(0.4)	2	(0.5)	0.79 (0.07,8.81)	0.852

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
14-3	Acne (Lifetime)	All	369 (47.5)	477 (40.6)	1.32 (1.10,1.59)	0.003
		Officer	128 (41.7)	194 (42.0)	0.99 (0.74,1.32)	0.935
		Enlisted Flyer	63 (47.4)	69 (37.3)	1.51 (0.96,2.38)	0.073
		Enlisted Groundcrew	178 (52.8)	214 (40.6)	1.64 (1.24,2.16)	<0.001
14-4	Post-SEA Acne	All	205 (26.4)	239 (20.4)	1.40 (1.13,1.73)	0.002
		Officer	53 (17.3)	74 (16.0)	1.09 (0.74,1.61)	0.649
		Enlisted Flyer	34 (25.6)	34 (18.4)	1.53 (0.89,2.61)	0.125
		Enlisted Groundcrew	118 (35.0)	131 (24.9)	1.62 (1.21,2.19)	0.001
14-5	Post-SEA Acne (No Pre-SEA Acne)	All	90 (18.0)	90 (11.4)	1.70 (1.24,2.34)	0.001
		Officer	18 (9.1)	25 (8.5)	1.08 (0.57,2.03)	0.817
		Enlisted Flyer	15 (17.6)	13 (10.1)	1.91 (0.86,4.25)	0.112
		Enlisted Groundcrew	57 (26.3)	52 (14.2)	2.14 (1.41,3.27)	<0.001
14-6	Post-SEA Acne (with Pre-SEA Acne)	All	115 (41.4)	149 (38.6)	1.12 (0.82,1.54)	0.473
		Officer	35 (31.8)	49 (29.0)	1.14 (0.68,1.92)	0.615
		Enlisted Flyer	19 (39.6)	21 (37.5)	1.09 (0.49,2.41)	0.828
		Enlisted Groundcrew	61 (50.8)	79 (49.1)	1.07 (0.67,1.72)	0.770
14-8	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (Excluding Participants with Pre-SEA Acne)	All	26 (29.5)	26 (29.2)	1.02 (0.53,1.94)	0.961
		Officer	2 (11.1)	5 (20.0)	0.50 (0.09,2.93)	0.442
		Enlisted Flyer	4 (28.6)	6 (50.0)	0.40 (0.08,2.02)	0.268
		Enlisted Groundcrew	20 (35.7)	15 (28.8)	1.37 (0.61,3.09)	0.447
14-10	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (All Post-SEA Occurrences)	All	74 (36.6)	82 (34.7)	1.09 (0.73,1.61)	0.681
		Officer	17 (32.1)	22 (30.1)	1.09 (0.51,2.35)	0.816
		Enlisted Flyer	13 (39.4)	16 (48.5)	0.69 (0.26,1.83)	0.458
		Enlisted Groundcrew	44 (37.9)	44 (33.8)	1.19 (0.71,2.01)	0.505
14-13	Acneiform Lesions	All	45 (5.8)	58 (4.9)	1.18 (0.79,1.77)	0.413
		Officer	12 (3.9)	13 (2.8)	1.40 (0.63,3.12)	0.404
		Enlisted Flyer	4 (3.0)	12 (6.5)	0.45 (0.14,1.42)	0.172
		Enlisted Groundcrew	29 (8.6)	33 (6.3)	1.41 (0.84,2.37)	0.195
14-14	Acneiform Scars	All	52 (6.7)	72 (6.1)	1.10 (0.76,1.59)	0.621
		Officer	18 (5.9)	19 (4.1)	1.45 (0.75,2.81)	0.269
		Enlisted Flyer	14 (10.5)	12 (6.5)	1.70 (0.76,3.80)	0.199
		Enlisted Groundcrew	20 (5.9)	41 (7.8)	0.75 (0.43,1.30)	0.303
14-15	Comedones	All	41 (5.3)	79 (6.7)	0.77 (0.52,1.14)	0.187
		Officer	9 (2.9)	28 (6.1)	0.47 (0.22,1.01)	0.052
		Enlisted Flyer	11 (8.3)	21 (11.4)	0.70 (0.33,1.52)	0.370
		Enlisted Groundcrew	21 (6.2)	30 (5.7)	1.10 (0.62,1.96)	0.743

Table G-5. *Summary of Unadjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)*

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
14-16	Depigmentation	All	17 (2.2)	36 (3.1)	0.71 (0.39,1.27)	0.236
		Officer	6 (2.0)	10 (2.2)	0.90 (0.32,2.51)	0.842
		Enlisted Flyer	5 (3.8)	6 (3.2)	1.17 (0.35,3.90)	0.804
		Enlisted Groundcrew	6 (1.8)	20 (3.8)	0.46 (0.18,1.16)	0.099
14-17	Hyperpigmentation	All	53 (6.8)	94 (8.0)	0.84 (0.59,1.19)	0.329
		Officer	17 (5.5)	33 (7.1)	0.76 (0.42,1.39)	0.378
		Enlisted Flyer	10 (7.5)	17 (9.2)	0.80 (0.36,1.82)	0.599
		Enlisted Groundcrew	26 (7.7)	44 (8.3)	0.92 (0.55,1.52)	0.739
14-18	Inclusion Cysts	All	98 (12.6)	134 (11.4)	1.12 (0.85,1.48)	0.425
		Officer	27 (8.8)	55 (11.9)	0.71 (0.44,1.16)	0.173
		Enlisted Flyer	23 (17.3)	22 (11.9)	1.55 (0.82,2.92)	0.175
		Enlisted Groundcrew	48 (14.2)	57 (10.8)	1.37 (0.91,2.07)	0.134
14-19	Dermatology Index	All	184 (23.7)	277 (23.6)	1.00 (0.81,1.24)	0.965
		Officer	54 (17.6)	94 (20.3)	0.84 (0.58,1.21)	0.343
		Enlisted Flyer	40 (30.1)	49 (26.5)	1.19 (0.73,1.96)	0.482
		Enlisted Groundcrew	90 (26.7)	134 (25.4)	1.07 (0.78,1.46)	0.676
15-3	Essential Hypertension	All	412 (54.3)	644 (56.2)	0.93 (0.77,1.11)	0.411
		Officer	154 (51.7)	258 (57.5)	0.79 (0.59,1.06)	0.120
		Enlisted Flyer	78 (59.5)	110 (60.4)	0.96 (0.61,1.52)	0.873
		Enlisted Groundcrew	180 (54.5)	276 (53.6)	1.04 (0.79,1.37)	0.786
15-4	Heart Disease (Excluding Essential Hypertension)	All	644 (84.0)	937 (81.1)	1.22 (0.96,1.56)	0.101
		Officer	253 (83.8)	388 (85.7)	0.86 (0.58,1.29)	0.481
		Enlisted Flyer	120 (91.6)	149 (81.0)	2.56 (1.25,5.26)	0.010
		Enlisted Groundcrew	271 (81.1)	400 (77.1)	1.28 (0.91,1.80)	0.158
15-5	Myocardial Infarction	All	77 (10.0)	132 (11.4)	0.87 (0.64,1.17)	0.339
		Officer	28 (9.3)	53 (11.7)	0.77 (0.48,1.25)	0.292
		Enlisted Flyer	15 (11.5)	27 (14.7)	0.75 (0.38,1.48)	0.408
		Enlisted Groundcrew	34 (10.2)	52 (10.0)	1.02 (0.65,1.61)	0.939
15-6	Stroke or Transient Ischemic Attack	All	29 (3.8)	36 (3.1)	1.22 (0.74,2.01)	0.431
		Officer	13 (4.3)	16 (3.5)	1.23 (0.58,2.59)	0.589
		Enlisted Flyer	6 (4.6)	7 (3.8)	1.21 (0.40,3.70)	0.733
		Enlisted Groundcrew	10 (3.0)	13 (2.5)	1.20 (0.52,2.77)	0.667
15-8	Systolic Blood Pressure	All	175 (22.8)	301 (26.0)	0.84 (0.68,1.04)	0.111
		Officer	78 (25.9)	128 (28.3)	0.89 (0.64,1.23)	0.480
		Enlisted Flyer	30 (22.9)	52 (28.3)	0.75 (0.45,1.27)	0.286
		Enlisted Groundcrew	67 (20.1)	121 (23.3)	0.83 (0.59,1.16)	0.263
15-10	Diastolic Blood Pressure	All	41 (5.4)	56 (4.8)	1.11 (0.73,1.68)	0.619
		Officer	11 (3.7)	19 (4.2)	0.87 (0.41,1.85)	0.711
		Enlisted Flyer	7 (5.3)	10 (5.4)	0.98 (0.36,2.65)	0.972
		Enlisted Groundcrew	23 (6.9)	27 (5.2)	1.35 (0.76,2.39)	0.308

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
15-11	Heart Sounds	All	53 (6.9)	69 (6.0)	1.17 (0.81,1.70)	0.405
		Officer	22 (7.3)	36 (7.9)	0.91 (0.53,1.59)	0.748
		Enlisted Flyer	10 (7.6)	8 (4.3)	1.82 (0.70,4.74)	0.221
		Enlisted Groundcrew	21 (6.3)	25 (4.8)	1.33 (0.73,2.41)	0.355
15-12	Overall ECG	All	276 (36.0)	409 (35.4)	1.03 (0.85,1.24)	0.771
		Officer	119 (39.5)	183 (40.4)	0.96 (0.72,1.30)	0.813
		Enlisted Flyer	62 (47.3)	70 (38.0)	1.46 (0.93,2.30)	0.100
		Enlisted Groundcrew	95 (28.4)	156 (30.1)	0.92 (0.68,1.25)	0.614
15-13	ECG: RBBB	All	32 (4.2)	42 (3.6)	1.16 (0.72,1.85)	0.545
		Officer	15 (5.0)	15 (3.3)	1.53 (0.74,3.18)	0.253
		Enlisted Flyer	9 (6.9)	12 (6.5)	1.06 (0.43,2.59)	0.903
		Enlisted Groundcrew	8 (2.4)	15 (2.9)	0.82 (0.35,1.97)	0.664
15-14	ECG: LBBB	All	8 (1.0)	16 (1.4)	0.75 (0.32,1.77)	0.507
		Officer	1 (0.3)	10 (2.2)	0.15 (0.02,1.16)	0.069
		Enlisted Flyer	3 (2.3)	0 (0.0)	--	0.141[a]
		Enlisted Groundcrew	4 (1.2)	6 (1.2)	1.04 (0.29,3.70)	0.956
15-15	ECG: Nonspecific ST- and T-wave Changes	All	180 (23.5)	269 (23.3)	1.01 (0.82,1.26)	0.908
		Officer	68 (22.6)	114 (25.2)	0.87 (0.62,1.22)	0.419
		Enlisted Flyer	44 (33.6)	48 (26.1)	1.43 (0.88,2.34)	0.150
		Enlisted Groundcrew	68 (20.4)	107 (20.6)	0.98 (0.70,1.38)	0.928
15-16	ECG: Bradycardia	All	44 (5.7)	51 (4.4)	1.32 (0.87,2.00)	0.190
		Officer	24 (8.0)	26 (5.7)	1.42 (0.80,2.53)	0.229
		Enlisted Flyer	8 (6.1)	4 (2.2)	2.93 (0.86,9.93)	0.085
		Enlisted Groundcrew	12 (3.6)	21 (4.0)	0.88 (0.43,1.82)	0.738
15-17	ECG: Tachycardia	All	3 (0.4)	7 (0.6)	0.65 (0.17,2.50)	0.516
		Officer	0 (0.0)	1 (0.2)	--	0.999[a]
		Enlisted Flyer	0 (0.0)	1 (0.5)	--	0.999[a]
		Enlisted Groundcrew	3 (0.9)	5 (1.0)	0.93 (0.22,3.92)	0.923
15-18	ECG: Arrhythmia	All	73 (9.5)	125 (10.8)	0.87 (0.64,1.18)	0.363
		Officer	39 (13.0)	60 (13.2)	0.98 (0.63,1.50)	0.909
		Enlisted Flyer	10 (7.6)	22 (12.0)	0.61 (0.28,1.33)	0.214
		Enlisted Groundcrew	24 (7.2)	43 (8.3)	0.86 (0.51,1.44)	0.560
15-19	ECG: Evidence of Prior Myocardial Infarction	All	34 (4.4)	61 (5.3)	0.83 (0.54,1.28)	0.404
		Officer	18 (6.0)	27 (6.0)	1.00 (0.54,1.86)	0.991
		Enlisted Flyer	7 (5.3)	15 (8.2)	0.64 (0.25,1.61)	0.338
		Enlisted Groundcrew	9 (2.7)	19 (3.7)	0.73 (0.33,1.63)	0.441
15-20	Funduscopic Examination	All	80 (11.5)	107 (10.1)	1.16 (0.85,1.57)	0.354
		Officer	25 (9.3)	36 (8.7)	1.08 (0.63,1.84)	0.789
		Enlisted Flyer	16 (13.4)	21 (12.4)	1.09 (0.55,2.20)	0.799
		Enlisted Groundcrew	39 (12.6)	50 (10.4)	1.24 (0.79,1.93)	0.348

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
15-21	Carotid Bruits	All	15 (2.0)	29 (2.5)	0.78 (0.41,1.46)	0.425
		Officer	6 (2.0)	17 (3.8)	0.52 (0.20,1.34)	0.176
		Enlisted Flyer	3 (2.3)	4 (2.2)	1.05 (0.23,4.79)	0.945
		Enlisted Groundcrew	6 (1.8)	8 (1.5)	1.17 (0.40,3.40)	0.775
15-22	Radial Pulses	All	48 (6.3)	82 (7.1)	0.87 (0.60,1.26)	0.458
		Officer	22 (7.3)	32 (7.1)	1.03 (0.59,1.81)	0.915
		Enlisted Flyer	4 (3.1)	12 (6.6)	0.45 (0.14,1.42)	0.171
		Enlisted Groundcrew	22 (6.6)	38 (7.4)	0.89 (0.52,1.53)	0.671
15-23	Femoral Pulses	All	13 (1.7)	9 (0.8)	2.20 (0.93,5.17)	0.068
		Officer	4 (1.3)	5 (1.1)	1.20 (0.32,4.52)	0.785
		Enlisted Flyer	4 (3.1)	2 (1.1)	2.87 (0.52,15.89)	0.228
		Enlisted Groundcrew	5 (1.5)	2 (0.4)	3.93 (0.76,20.37)	0.103
15-24	Popliteal Pulses	All	18 (2.4)	30 (2.6)	0.90 (0.50,1.63)	0.736
		Officer	7 (2.3)	15 (3.3)	0.70 (0.28,1.73)	0.433
		Enlisted Flyer	5 (3.8)	7 (3.8)	1.01 (0.31,3.26)	0.985
		Enlisted Groundcrew	6 (1.8)	8 (1.5)	1.17 (0.40,3.39)	0.778
15-25	Dorsalis Pedis Pulses	All	61 (8.0)	96 (8.3)	0.95 (0.68,1.33)	0.778
		Officer	24 (8.0)	45 (10.0)	0.78 (0.47,1.32)	0.359
		Enlisted Flyer	10 (7.6)	18 (9.8)	0.76 (0.34,1.70)	0.501
		Enlisted Groundcrew	27 (8.1)	33 (6.4)	1.29 (0.76,2.19)	0.341
15-26	Posterior Tibial Pulses	All	33 (4.3)	68 (5.9)	0.72 (0.47,1.10)	0.124
		Officer	11 (3.6)	31 (6.9)	0.51 (0.25,1.04)	0.062
		Enlisted Flyer	8 (6.2)	11 (6.0)	1.03 (0.40,2.65)	0.945
		Enlisted Groundcrew	14 (4.2)	26 (5.0)	0.83 (0.43,1.61)	0.582
15-27	Leg Pulses	All	66 (8.7)	114 (9.9)	0.86 (0.63,1.18)	0.358
		Officer	25 (8.3)	54 (12.0)	0.67 (0.41,1.10)	0.113
		Enlisted Flyer	12 (9.3)	20 (10.9)	0.84 (0.40,1.79)	0.653
		Enlisted Groundcrew	29 (8.7)	40 (7.7)	1.13 (0.69,1.87)	0.622
15-28	Peripheral Pulses	All	106 (13.9)	182 (15.9)	0.86 (0.66,1.11)	0.239
		Officer	43 (14.4)	81 (18.1)	0.76 (0.51,1.14)	0.190
		Enlisted Flyer	15 (11.6)	31 (17.0)	0.64 (0.33,1.24)	0.188
		Enlisted Groundcrew	48 (14.4)	70 (13.6)	1.07 (0.72,1.59)	0.749
15-30	Resting Pressure Index	All	32 (4.2)	40 (3.5)	1.20 (0.75,1.93)	0.449
		Officer	13 (4.3)	21 (4.7)	0.92 (0.45,1.86)	0.807
		Enlisted Flyer	8 (6.1)	7 (3.8)	1.63 (0.57,4.60)	0.360
		Enlisted Groundcrew	11 (3.3)	12 (2.4)	1.42 (0.62,3.27)	0.404
15-32	Hyperemic Pressure Index (1 Minute Post-exercise)	All	72 (9.7)	103 (9.3)	1.05 (0.77,1.44)	0.755
		Officer	21 (7.1)	35 (8.0)	0.88 (0.50,1.54)	0.653
		Enlisted Flyer	22 (17.9)	23 (13.0)	1.46 (0.77,2.76)	0.245
		Enlisted Groundcrew	29 (9.0)	45 (9.1)	0.99 (0.61,1.61)	0.963
15-34	Hyperemic Pressure Index (2 Minutes Post-exercise)	All	34 (4.6)	65 (5.9)	0.77 (0.51,1.19)	0.234
		Officer	11 (3.7)	28 (6.4)	0.57 (0.28,1.16)	0.120
		Enlisted Flyer	8 (6.5)	13 (7.3)	0.88 (0.35,2.19)	0.779
		Enlisted Groundcrew	15 (4.6)	24 (4.8)	0.96 (0.49,1.85)	0.898

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
15-35	Intermittent Claudication and Vascular Insufficiency Index	All	22 (2.9)	37 (3.2)	0.89 (0.52,1.52)	0.673
		Officer	8 (2.6)	13 (2.9)	0.92 (0.38,2.25)	0.857
		Enlisted Flyer	4 (3.1)	5 (2.7)	1.13 (0.30,4.28)	0.860
		Enlisted Groundcrew	10 (3.0)	19 (3.7)	0.81 (0.37,1.76)	0.593
16-13	RBC Morphology	All	51 (6.6)	61 (5.2)	1.29 (0.88,1.89)	0.197
		Officer	18 (5.9)	31 (6.7)	0.86 (0.47,1.58)	0.635
		Enlisted Flyer	10 (7.5)	10 (5.4)	1.42 (0.57,3.52)	0.446
		Enlisted Groundcrew	23 (6.9)	20 (3.8)	1.88 (1.02,3.49)	0.044
16-16	Absolute Neutrophils (Bands) (Zero vs. Nonzero)	All	145 (18.8)	239 (20.4)	0.90 (0.72,1.14)	0.384
		Officer	52 (17.0)	92 (20.0)	0.82 (0.56,1.19)	0.297
		Enlisted Flyer	24 (18.0)	41 (22.2)	0.77 (0.44,1.36)	0.370
		Enlisted Groundcrew	69 (20.8)	106 (20.2)	1.04 (0.74,1.46)	0.823
16-20	Absolute Eosinophils (Zero vs. Nonzero)	All	72 (9.3)	126 (10.8)	0.85 (0.63,1.16)	0.309
		Officer	25 (8.2)	50 (10.9)	0.73 (0.44,1.21)	0.220
		Enlisted Flyer	13 (9.8)	16 (8.6)	1.14 (0.53,2.47)	0.731
		Enlisted Groundcrew	34 (10.2)	60 (11.4)	0.89 (0.57,1.38)	0.595
16-22	Absolute Basophils (Zero vs. Nonzero)	All	374 (48.5)	551 (47.1)	1.06 (0.88,1.27)	0.530
		Officer	142 (46.4)	223 (48.5)	0.92 (0.69,1.23)	0.574
		Enlisted Flyer	58 (43.6)	84 (45.4)	0.93 (0.59,1.46)	0.751
		Enlisted Groundcrew	174 (52.4)	244 (46.4)	1.27 (0.97,1.68)	0.086
16-24	Fibrinogen	All	49 (6.4)	62 (5.3)	1.22 (0.83,1.79)	0.324
		Officer	16 (5.2)	16 (3.5)	1.54 (0.76,3.12)	0.235
		Enlisted Flyer	12 (9.0)	16 (8.6)	1.05 (0.48,2.29)	0.908
		Enlisted Groundcrew	21 (6.3)	30 (5.7)	1.12 (0.63,1.98)	0.708
16-26	Erythrocyte Sedimentation Rate	All	90 (11.7)	117 (10.0)	1.19 (0.89,1.59)	0.242
		Officer	31 (10.1)	36 (7.8)	1.33 (0.80,2.20)	0.270
		Enlisted Flyer	20 (15.0)	21 (11.4)	1.38 (0.72,2.67)	0.335
		Enlisted Groundcrew	39 (11.7)	60 (11.4)	1.03 (0.67,1.59)	0.879
17-3	Occurrence of Kidney Stones	All	86 (11.2)	119 (10.2)	1.11 (0.82,1.48)	0.505
		Officer	42 (13.9)	47 (10.3)	1.40 (0.90,2.18)	0.137
		Enlisted Flyer	15 (11.4)	21 (11.5)	0.99 (0.49,2.00)	0.975
		Enlisted Groundcrew	29 (8.7)	51 (9.8)	0.88 (0.55,1.42)	0.610
17-4	Occurrence of Past Kidney Disease	All	271 (35.5)	436 (37.8)	0.91 (0.75,1.10)	0.307
		Officer	104 (34.4)	164 (36.5)	0.91 (0.67,1.24)	0.558
		Enlisted Flyer	53 (41.1)	64 (35.0)	1.30 (0.82,2.06)	0.273
		Enlisted Groundcrew	114 (34.3)	208 (39.9)	0.79 (0.59,1.05)	0.101
17-9	Urinary Microal-bumin to Urinary Creatinine Ratio (Nonzero vs. Zero)	All	106 (13.6)	141 (12.0)	1.16 (0.88,1.52)	0.290
		Officer	31 (10.1)	45 (9.7)	1.04 (0.64,1.69)	0.871
		Enlisted Flyer	25 (18.8)	23 (12.4)	1.63 (0.88,3.02)	0.120
		Enlisted Groundcrew	50 (14.8)	73 (13.9)	1.08 (0.73,1.60)	0.686

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
17-11	Urinary Occult Blood	All	22 (2.8)	25 (2.1)	1.34 (0.75,2.39)	0.326
		Officer	13 (4.2)	9 (1.9)	2.23 (0.94,5.27)	0.069
		Enlisted Flyer	2 (1.5)	3 (1.6)	0.93 (0.15,5.62)	0.934
		Enlisted Groundcrew	7 (2.1)	13 (2.5)	0.84 (0.33,2.12)	0.711
17-12	Urinary WBC Count	All	55 (7.1)	65 (5.5)	1.30 (0.90,1.88)	0.168
		Officer	18 (5.9)	24 (5.2)	1.14 (0.61,2.13)	0.690
		Enlisted Flyer	7 (5.3)	7 (3.8)	1.41 (0.48,4.13)	0.528
		Enlisted Groundcrew	30 (8.9)	34 (6.5)	1.42 (0.85,2.36)	0.182
17-13	Urinary Protein	All	26 (3.3)	49 (4.2)	0.79 (0.49,1.29)	0.348
		Officer	7 (2.3)	14 (3.0)	0.75 (0.30,1.87)	0.533
		Enlisted Flyer	5 (3.8)	7 (3.8)	0.99 (0.31,3.20)	0.991
		Enlisted Groundcrew	14 (4.2)	28 (5.3)	0.77 (0.40,1.49)	0.441
18-3	Past Thyroid Disease	All	83 (10.8)	152 (13.0)	0.81 (0.61,1.07)	0.136
		Officer	36 (11.8)	60 (13.1)	0.89 (0.57,1.39)	0.616
		Enlisted Flyer	14 (10.6)	24 (13.0)	0.80 (0.39,1.60)	0.523
		Enlisted Groundcrew	33 (9.9)	68 (13.0)	0.73 (0.47,1.14)	0.168
18-4	Composite Diabetes Indicator (2002 AFHS Diabetes Definition)	All	141 (18.2)	226 (19.3)	0.93 (0.74,1.17)	0.544
		Officer	50 (16.3)	79 (17.1)	0.95 (0.64,1.40)	0.783
		Enlisted Flyer	29 (21.8)	43 (23.2)	0.92 (0.54,1.57)	0.762
		Enlisted Groundcrew	62 (18.4)	104 (19.8)	0.91 (0.65,1.30)	0.617
18-5	Composite Diabetes Indicator (Pre-2002 AFHS Diabetes Definition)	All	160 (20.6)	259 (22.1)	0.92 (0.73,1.14)	0.441
		Officer	61 (19.9)	85 (18.4)	1.10 (0.77,1.59)	0.595
		Enlisted Flyer	31 (23.3)	51 (27.6)	0.80 (0.48,1.34)	0.392
		Enlisted Groundcrew	68 (20.2)	123 (23.4)	0.83 (0.59,1.16)	0.269
18-8	Time to Diabetes Onset (years) (2002 AFHS Diabetes Definition)	All	27.67[b]	28.41[b]	0.89 (0.72,1.10)[c]	0.265[c]
		Officer	28.08[b]	28.16[b]	0.91 (0.64,1.30)[c]	0.613[c]
		Enlisted Flyer	27.09[b]	27.08[b]	0.85 (0.53,1.36)[c]	0.496[c]
		Enlisted Groundcrew	27.83[b]	28.92[b]	0.89 (0.65,1.22)[c]	0.459[c]
18-9	Time to Diabetes Onset (years) (Pre-2002 AFHS Diabetes Definition)	All	27.67[b]	28.41[b]	0.86 (0.70,1.04)[c]	0.126[c]
		Officer	28.08[b]	28.16[b]	1.00 (0.72,1.40)[c]	0.987[c]
		Enlisted Flyer	27.09[b]	27.08[b]	0.73 (0.47,1.15)[c]	0.173[c]
		Enlisted Groundcrew	27.83[b]	28.92[b]	0.82 (0.61,1.10)[c]	0.180[c]
18-10	Thyroid Gland	All	8 (1.1)	24 (2.2)	0.49 (0.22,1.10)	0.069
		Officer	3 (1.1)	8 (1.9)	0.55 (0.14,2.09)	0.381
		Enlisted Flyer	0 (0.0)	3 (1.7)	--	0.372[a]
		Enlisted Groundcrew	5 (1.5)	13 (2.6)	0.59 (0.21,1.66)	0.313
18-11	Testicular Examination	All	56 (7.3)	78 (6.7)	1.10 (0.77,1.56)	0.618
		Officer	21 (7.0)	34 (7.5)	0.93 (0.53,1.64)	0.807
		Enlisted Flyer	14 (10.7)	13 (7.2)	1.55 (0.70,3.41)	0.280
		Enlisted Groundcrew	21 (6.3)	31 (5.9)	1.07 (0.60,1.89)	0.826

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
18-15	Free T_4	All	67 (9.1)	113 (10.4)	0.87 (0.63,1.19)	0.384
		Officer	29 (10.2)	36 (8.6)	1.21 (0.72,2.02)	0.468
		Enlisted Flyer	7 (5.6)	24 (13.8)	0.37 (0.15,0.88)	0.025
		Enlisted Groundcrew	31 (9.6)	53 (10.7)	0.89 (0.56,1.42)	0.616
18-16	Anti-thyroid Antibodies	All	4 (0.5)	6 (0.6)	0.99 (0.28,3.52)	0.988
		Officer	2 (0.7)	3 (0.7)	0.98 (0.16,5.92)	0.985
		Enlisted Flyer	2 (1.6)	1 (0.6)	2.79 (0.25,31.12)	0.404
		Enlisted Groundcrew	0 (0.0)	2 (0.4)	--	0.676[a]
18-18	Fasting Glucose	All	164 (21.1)	236 (20.1)	1.06 (0.85,1.33)	0.588
		Officer	60 (19.6)	85 (18.4)	1.08 (0.75,1.56)	0.675
		Enlisted Flyer	30 (22.6)	44 (23.8)	0.93 (0.55,1.58)	0.798
		Enlisted Groundcrew	74 (22.0)	107 (20.3)	1.10 (0.79,1.54)	0.569
18-20	2-hour Postprandial Glucose (Nondiabetics Only)	All	133 (21.1)	198 (21.2)	1.00 (0.78,1.28)	0.997
		Officer	54 (21.3)	65 (17.2)	1.30 (0.87,.194)	0.201
		Enlisted Flyer	28 (27.5)	39 (27.9)	0.98 (0.55,1.73)	0.944
		Enlisted Groundcrew	51 (18.7)	94 (22.5)	0.79 (0.54,1.16)	0.230
18-21	2-hour Postprandial Urinary Glucose (Nondiabetics Only)	All	171 (27.2)	242 (25.9)	1.07 (0.85,1.35)	0.558
		Officer	60 (23.6)	67 (17.7)	1.44 (0.97,2.12)	0.070
		Enlisted Flyer	33 (32.4)	45 (32.1)	1.01 (0.58,1.74)	0.972
		Enlisted Groundcrew	78 (28.6)	130 (31.1)	0.89 (0.63,1.24)	0.479
18-27	Hemoglobin A1c (Diabetics Only)	All	90 (64.7)	146 (66.1)	0.94 (0.60,1.47)	0.798
		Officer	27 (54.0)	44 (57.9)	0.85 (0.42,1.75)	0.666
		Enlisted Flyer	18 (64.3)	29 (69.0)	0.81 (0.29,2.22)	0.678
		Enlisted Groundcrew	45 (73.8)	73 (70.9)	1.16 (0.57,2.35)	0.690
18-29	C-peptide (Diabetics Only)	All	36 (25.9)	56 (25.3)	1.03 (0.63,1.67)	0.906
		Officer	15 (30.0)	14 (18.4)	1.90 (0.82,4.39)	0.134
		Enlisted Flyer	4 (14.3)	12 (28.6)	0.42 (0.12,1.46)	0.171
		Enlisted Groundcrew	17 (27.9)	30 (29.1)	0.94 (0.47,1.90)	0.863
18-31	Proinsulin (Diabetics Only)	All	73 (52.5)	104 (47.1)	1.24 (0.81,1.90)	0.313
		Officer	25 (50.0)	28 (36.8)	1.71 (0.83,3.54)	0.145
		Enlisted Flyer	12 (42.9)	23 (54.8)	0.62 (0.24,1.62)	0.330
		Enlisted Groundcrew	36 (59.0)	53 (51.5)	1.36 (0.72,2.58)	0.348
18-32	GADA (Diabetics Only)	All	3 (2.2)	9 (4.1)	0.52 (0.14,1.95)	0.310
		Officer	2 (4.0)	3 (3.9)	1.01 (0.16,6.29)	0.988
		Enlisted Flyer	0 (0.0)	2 (4.8)	--	0.660[a]
		Enlisted Groundcrew	1 (1.6)	4 (3.9)	0.41 (0.05,3.78)	0.433
18-34	Total Testosterone	All	128 (16.6)	165 (14.2)	1.20 (0.94,1.55)	0.150
		Officer	54 (17.8)	63 (13.8)	1.36 (0.91,2.02)	0.132
		Enlisted Flyer	21 (15.9)	25 (13.7)	1.19 (0.63,2.23)	0.591
		Enlisted Groundcrew	53 (15.8)	77 (14.8)	1.09 (0.74,1.59)	0.670

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal				Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand		Comparison			
18-36	Free Testosterone	All	49	(6.4)	64	(5.5)	1.16 (0.79,1.71)	0.437
		Officer	28	(9.2)	23	(5.0)	1.92 (1.08,3.40)	0.025
		Enlisted Flyer	9	(6.8)	17	(9.3)	0.71 (0.31,1.65)	0.425
		Enlisted Groundcrew	12	(3.6)	24	(4.6)	0.77 (0.38,1.56)	0.471
18-38	Estradiol	All	23	(3.0)	30	(2.6)	1.16 (0.67,2.01)	0.597
		Officer	11	(3.6)	10	(2.2)	1.68 (0.71,4.02)	0.240
		Enlisted Flyer	2	(1.5)	8	(4.4)	0.33 (0.07,1.60)	0.171
		Enlisted Groundcrew	10	(3.0)	12	(2.3)	1.31 (0.56,3.06)	0.537
18-40	LH	All	35	(4.5)	69	(5.9)	0.75 (0.50,1.14)	0.179
		Officer	14	(4.6)	29	(6.3)	0.71 (0.37,1.38)	0.315
		Enlisted Flyer	6	(4.5)	12	(6.6)	0.67 (0.25,1.85)	0.443
		Enlisted Groundcrew	15	(4.5)	28	(5.4)	0.83 (0.43,1.57)	0.562
18-42	FSH	All	44	(5.7)	70	(6.0)	0.94 (0.64,1.39)	0.773
		Officer	26	(8.6)	33	(7.2)	1.21 (0.71,2.06)	0.493
		Enlisted Flyer	9	(6.8)	15	(8.2)	0.81 (0.35,1.92)	0.640
		Enlisted Groundcrew	9	(2.7)	22	(4.2)	0.63 (0.29,1.38)	0.246
19-14	Lupus Panel: ANA Test	All	133	(19.1)	204	(19.1)	1.00 (0.79,1.28)	0.985
		Officer	52	(18.8)	88	(21.1)	0.87 (0.59,1.27)	0.468
		Enlisted Flyer	20	(17.2)	28	(16.8)	1.03 (0.55,1.94)	0.917
		Enlisted Groundcrew	61	(20.1)	88	(18.2)	1.13 (0.79,1.63)	0.497
19-15	Lupus Panel: Thyroid Microsomal Antibody	All	23	(3.3)	24	(2.2)	1.49 (0.83,2.66)	0.181
		Officer	9	(3.3)	10	(2.4)	1.37 (0.55,3.42)	0.498
		Enlisted Flyer	2	(1.7)	4	(2.4)	0.71 (0.13,3.97)	0.701
		Enlisted Groundcrew	12	(4.0)	10	(2.1)	1.95 (0.83,4.58)	0.123
19-16	Lupus Panel: MSK Antismooth Muscle Antibody	All	9	(1.3)	8	(0.7)	1.74 (0.67,4.53)	0.258
		Officer	6	(2.2)	2	(0.5)	4.61 (0.92,23.01)	0.062
		Enlisted Flyer	1	(0.9)	3	(1.8)	0.48 (0.05,4.63)	0.522
		Enlisted Groundcrew	2	(0.7)	3	(0.6)	1.07 (0.18,6.41)	0.945
19-17	Lupus Panel: MSK Antimitochondrial Antibody	All	2	(0.3)	2	(0.2)	1.54 (0.22,10.95)	0.668
		Officer	2	(0.7)	1	(0.2)	3.04 (0.27,33.65)	0.365
		Enlisted Flyer	0	(0.0)	1	(0.6)	--	0.999[a]
		Enlisted Groundcrew	0	(0.0)	0	(0.0)	--	--
19-18	Lupus Panel: MSK Antiparietal Cell Antibody	All	16	(2.3)	33	(3.1)	0.74 (0.40,1.35)	0.320
		Officer	8	(2.9)	7	(1.7)	1.75 (0.63,4.88)	0.286
		Enlisted Flyer	1	(0.9)	5	(3.0)	0.28 (0.03,2.44)	0.250
		Enlisted Groundcrew	7	(2.3)	21	(4.3)	0.52 (0.22,1.24)	0.141
19-19	Lupus Panel: Rheumatoid Factor	All	166	(23.9)	216	(20.2)	1.24 (0.98,1.56)	0.069
		Officer	62	(22.5)	67	(16.1)	1.51 (1.03,2.22)	0.035
		Enlisted Flyer	28	(24.1)	44	(26.3)	0.89 (0.51,1.54)	0.675
		Enlisted Groundcrew	76	(25.1)	105	(21.7)	1.21 (0.86,1.69)	0.272

Table Ref.	Clinical Parameter	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
			Ranch Hand	Comparison		
20-3	Asthma	All	50 (6.5)	75 (6.4)	1.01 (0.70,1.47)	0.938
		Officer	21 (6.9)	29 (6.3)	1.10 (0.62,1.97)	0.741
		Enlisted Flyer	5 (3.8)	15 (8.1)	0.45 (0.16,1.27)	0.131
		Enlisted Groundcrew	24 (7.2)	31 (5.9)	1.23 (0.71,2.14)	0.457
20-4	Bronchitis	All	242 (32.0)	352 (30.6)	1.07 (0.88,1.30)	0.510
		Officer	89 (30.1)	139 (30.8)	0.97 (0.70,1.33)	0.842
		Enlisted Flyer	47 (37.0)	52 (28.7)	1.46 (0.90,2.36)	0.126
		Enlisted Groundcrew	106 (31.8)	161 (31.1)	1.04 (0.77,1.39)	0.818
20-5	Pneumonia	All	97 (13.2)	161 (14.2)	0.92 (0.70,1.20)	0.520
		Officer	39 (13.4)	67 (15.2)	0.87 (0.57,1.33)	0.512
		Enlisted Flyer	24 (19.7)	20 (11.4)	1.91 (1.00,3.64)	0.049
		Enlisted Groundcrew	34 (10.5)	74 (14.3)	0.70 (0.45,1.08)	0.103
20-6	Thorax and Lung Abnormality	All	159 (20.5)	197 (16.8)	1.28 (1.01,1.61)	0.039
		Officer	38 (12.4)	54 (11.7)	1.07 (0.69,1.67)	0.760
		Enlisted Flyer	44 (33.1)	42 (22.7)	1.68 (1.02,2.77)	0.041
		Enlisted Groundcrew	77 (22.8)	101 (19.2)	1.25 (0.89,1.74)	0.192
20-7	X-ray Interpretation	All	119 (15.4)	205 (17.5)	0.86 (0.67,1.10)	0.224
		Officer	43 (14.1)	81 (17.5)	0.77 (0.52,1.15)	0.207
		Enlisted Flyer	27 (20.3)	33 (17.8)	1.17 (0.67,2.07)	0.580
		Enlisted Groundcrew	49 (14.6)	91 (17.3)	0.82 (0.56,1.19)	0.297
20-9	FVC	All	71 (9.2)	116 (10.0)	0.92 (0.67,1.25)	0.587
		Officer	22 (7.2)	33 (7.2)	1.01 (0.58,1.76)	0.980
		Enlisted Flyer	14 (10.8)	24 (13.1)	0.80 (0.40,1.61)	0.532
		Enlisted Groundcrew	35 (10.5)	59 (11.4)	0.91 (0.59,1.42)	0.686
20-11	FEV$_1$	All	241 (31.4)	341 (29.4)	1.10 (0.90,1.34)	0.347
		Officer	88 (28.9)	121 (26.4)	1.14 (0.82,1.57)	0.433
		Enlisted Flyer	56 (43.1)	68 (37.2)	1.28 (0.81,2.02)	0.292
		Enlisted Groundcrew	97 (29.0)	152 (29.3)	0.99 (0.73,1.34)	0.939

[a]P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormalities.

[b]10th percentile based on proportional hazards model was given for time to diabetes onset variable.

[c]Hazard ratio, confidence interval, and p-value, based on proportional hazards model, were given for time to diabetes onset variable.

--: Relative risk, confidence interval, and p-value were not presented because of the sparse number of participants with abnormalities.

Table G-6. Summary of Unadjusted Results for Dichotomous Variables – Model 2 (Ranch Hands: Log$_2$ (Initial Dioxin))

Table Ref.	Clinical Parameter	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
9-3	Self-perception of Health	1.10 (0.91,1.33)	0.314
9-4	Appearance of Illness or Distress	0.97 (0.67,1.39)	0.862
9-5	Relative Age Appearance	1.19 (0.92,1.54)	0.194
9-7	Body Mass Index	1.03 (0.90,1.19)	0.653
10-3	All Skin Neoplasms	0.82 (0.71,0.96)	0.011
10-4	Malignant Skin Neoplasms	0.81 (0.68,0.97)	0.021
10-5	Benign Skin Neoplasms	0.89 (0.77,1.04)	0.147
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	0.25 (0.05,1.16)	0.018
10-7	Basal Cell Carcinoma	0.72 (0.59,0.89)	0.001
10-8	Squamous Cell Carcinoma	0.82 (0.59,1.15)	0.246
10-9	Nonmelanoma	0.77 (0.64,0.93)	0.005
10-10	Melanoma	0.99 (0.63,1.55)	0.968
10-11	Systemic Neoplasms	0.90 (0.77,1.05)	0.160
10-12	Malignant Systemic Neoplasms	0.69 (0.54,0.88)	0.001
10-13	Benign Systemic Neoplasms	1.04 (0.88,1.23)	0.658
10-14	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	0.95 (0.54,1.66)	0.845
10-16	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	2.50 (0.70,8.93)	0.159
10-17	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	0.21 (0.04,1.19)	0.017
10-18	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	--	--
10-19	Malignant Systemic Neoplasms (Thyroid Gland)	0.19 (0.01,6.58)	0.194
10-20	Malignant Systemic Neoplasms (Bronchus and Lung)	0.70 (0.40,1.22)	0.179
10-21	All Stomach Neoplasms	1.37 (0.63,2.98)	0.442
10-22	Malignant Systemic Neoplasms (Colon and Rectum)	0.76 (0.44,1.32)	0.311
10-23	Malignant Systemic Neoplasms (Urinary System)	1.01 (0.62,1.63)	0.983
10-24	Malignant Systemic Neoplasms (Kidney and Ureter)	1.05 (0.47,2.33)	0.903
10-25	Malignant Systemic Neoplasms (Prostate)	0.54 (0.37,0.79)	<0.001
10-26	Malignant Systemic Neoplasms (Penis and Other Male Genital Organs)	2.15 (0.87,5.33)	0.103
10-27	Malignant Systemic Neoplasms (Testicles)	0.65 (0.22,1.92)	0.399
10-28	Malignant Systemic Neoplasms (Bone and Articular Cartilage)	--	--
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	2.50 (0.70,8.93)	0.159
10-30	Carcinoma in Situ	0.45 (0.12,1.65)	0.157
10-31	Hodgkin's Disease	--	--
10-32	Leukemia	--	--
10-33	Other Malignant Systemic Neoplasms (Lymphoid and Histiocytic Tissue)	0.67 (0.30,1.54)	0.312
10-34	Lymphoreticular Sarcoma	--	--
10-35	Skin and Systemic Neoplasms	0.82 (0.70,0.96)	0.011
10-36	Malignant Skin and Systemic Neoplasms	0.76 (0.64,0.90)	<0.001
10-38	PSA	0.58 (0.35,0.93)	0.013
11-3	Inflammatory Diseases	1.03 (0.49,2.16)	0.943
11-4	Hereditary and Degenerative Diseases	0.97 (0.80,1.18)	0.762
11-5	Peripheral Disorders	0.99 (0.85,1.17)	0.942
11-6	Other Neurological Disorders	1.07 (0.91,1.27)	0.403
11-7	Smell	0.38 (0.16,0.95)	0.012
11-8	Visual Fields	0.85 (0.39,1.85)	0.676
11-9	Light Reaction	3.98 (0.96,16.53)	0.039
11-10	Ocular Movement	0.82 (0.28,2.42)	0.712

Table Ref.	Clinical Parameter	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
11-11	Facial Sensation	0.59 (0.17,2.05)	0.359
11-12	Corneal Reflex	1.17 (0.24,5.76)	0.853
11-13	Smile	0.85 (0.45,1.59)	0.593
11-14	Palpebral Fissure	1.07 (0.70,1.62)	0.762
11-15	Balance	1.01 (0.64,1.60)	0.961
11-16	Gag Reflex	0.82 (0.20,3.35)	0.773
11-17	Speech	0.76 (0.36,1.60)	0.447
11-18	Tongue Position Relative to Midline	1.05 (0.45,2.45)	0.915
11-19	Shoulder Shrug	0.25 (0.03,2.53)	0.127
11-20	Cranial Nerve Index	0.85 (0.66,1.10)	0.214
11-21	Pinprick	1.23 (0.96,1.58)	0.099
11-22	Light Touch	1.22 (0.90,1.66)	0.204
11-23	Muscle Status	1.03 (0.75,1.41)	0.854
11-27	Babinski Reflex	0.86 (0.42,1.73)	0.655
11-28	Any Symmetric Peripheral Abnormality	0.94 (0.79,1.11)	0.436
11-29	Possible Peripheral Neuropathy	0.92 (0.77,1.09)	0.327
11-30	Probable Peripheral Neuropathy	1.01 (0.79,1.30)	0.920
11-31	Tremor	1.20 (0.92,1.56)	0.192
11-32	Coordination	1.31 (0.92,1.88)	0.148
11-33	Romberg Sign	1.01 (0.64,1.60)	0.961
11-34	Gait	0.92 (0.72,1.17)	0.479
11-35	CNS Index	1.00 (0.82,1.22)	0.993
12-3	Psychoses	1.05 (0.79,1.40)	0.719
12-4	Alcohol Dependence	1.08 (0.80,1.47)	0.626
12-5	Drug Dependence	--	--
12-6	Anxiety	1.13 (0.97,1.31)	0.128
12-7	Other Neuroses	1.07 (0.92,1.25)	0.369
12-8	SCL-90-R Anxiety	1.00 (0.79,1.26)	0.997
12-9	SCL-90-R Depression	1.05 (0.85,1.29)	0.673
12-10	SCL-90-R Hostility	1.31 (0.98,1.74)	0.077
12-11	SCL-90-R Interpersonal Sensitivity	1.13 (0.87,1.46)	0.366
12-12	SCL-90-R Obsessive-compulsive Behavior	1.15 (0.96,1.38)	0.140
12-13	SCL-90-R Paranoid Ideation	1.08 (0.74,1.59)	0.690
12-14	SCL-90-R Phobic Anxiety	1.10 (0.84,1.45)	0.491
12-15	SCL-90-R Psychoticism	1.14 (0.91,1.44)	0.260
12-16	SCL-90-R Somatization	1.20 (0.99,1.46)	0.066
12-17	SCL-90-R Global Severity	1.10 (0.89,1.36)	0.398
12-18	SCL-90-R Positive Symptom Total	1.02 (0.81,1.29)	0.865
12-19	SCL-90-R Positive Symptom Distress Index	1.09 (0.85,1.40)	0.489
13-3	Uncharacterized Hepatitis	1.21 (0.78,1.89)	0.410
13-4	Jaundice	0.74 (0.27,2.05)	0.545
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	1.46 (1.05,2.03)	0.029
13-6	Chronic Liver Disease and Cirrhosis (Nonalcohol-related)	1.00 (0.71,1.40)	0.979
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	1.28 (0.58,2.82)	0.557
13-8	Enlarged Liver	0.87 (0.58,1.30)	0.474
13-9	Other Disorders of the Liver	1.01 (0.87,1.17)	0.902
13-10	Current Hepatomegaly	0.79 (0.43,1.47)	0.438
13-12	AST	1.09 (0.85,1.41)	0.508
13-14	ALT	1.04 (0.80,1.34)	0.778

Table Ref.	Clinical Parameter	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
13-16	GGT	0.83 (0.65,1.05)	0.112
13-18	Alkaline Phosphatase	1.17 (0.91,1.51)	0.217
13-20	Total Bilirubin	0.77 (0.55,1.07)	0.101
13-21	Direct Bilirubin	--	--
13-23	LDH	0.76 (0.58,0.98)	0.028
13-25	Cholesterol	1.06 (0.83,1.34)	0.659
13-27	HDL Cholesterol	1.04 (0.87,1.25)	0.660
13-29	Cholesterol-HDL Ratio	1.11 (0.96,1.29)	0.163
13-31	Triglycerides	1.17 (0.97,1.40)	0.099
13-33	Creatine Phosphokinase	0.94 (0.72,1.22)	0.621
13-35	Serum Amylase	0.83 (0.53,1.30)	0.414
13-36	Antibodies for Hepatitis A	1.03 (0.88,1.20)	0.731
13-37	Serological Evidence of Prior Hepatitis B Infection	1.18 (0.92,1.51)	0.199
13-38	Antibodies for Hepatitis C	0.43 (0.08,2.25)	0.237
13-39	Stool Hemoccult	0.91 (0.48,1.73)	0.763
13-41	Prealbumin	1.17 (0.71,1.91)	0.540
13-43	Albumin	--	--
13-45	α-1-Acid Glycoprotein	0.89 (0.67,1.20)	0.449
13-49	α-2-Macroglobulin	0.92 (0.75,1.13)	0.427
13-51	Apolipoprotein B	1.03 (0.53,1.99)	0.929
13-53	C3 Complement	1.78 (0.49,6.39)	0.394
13-55	C4 Complement	1.43 (1.10,1.87)	0.009
13-57	Haptoglobin	0.86 (0.69,1.06)	0.156
13-59	Transferrin	1.32 (0.90,1.93)	0.169
13-61	Prothrombin Time	0.64 (0.27,1.56)	0.275
14-3	Acne (Lifetime)	0.95 (0.82,1.10)	0.466
14-4	Post-SEA Acne	1.04 (0.89,1.22)	0.641
14-5	Post-SEA Acne (No Pre-SEA Acne)	1.06 (0.86,1.31)	0.596
14-6	Post-SEA Acne (with Pre-SEA Acne)	1.10 (0.85,1.43)	0.472
14-8	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (Excluding Participants with Pre-SEA Acne)	1.37 (0.91,2.07)	0.135
14-10	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (All Post-SEA Occurrences)	1.05 (0.79,1.40)	0.736
14-13	Acneiform Lesions	1.36 (1.01,1.84)	0.050
14-14	Acneiform Scars	1.08 (0.79,1.46)	0.640
14-15	Comedones	1.31 (0.96,1.79)	0.094
14-16	Depigmentation	1.06 (0.69,1.62)	0.800
14-17	Hyperpigmentation	0.80 (0.61,1.06)	0.114
14-18	Inclusion Cysts	1.10 (0.89,1.36)	0.373
14-19	Dermatology Index	1.20 (1.01,1.41)	0.034
15-3	Essential Hypertension	1.08 (0.92,1.26)	0.331
15-4	Heart Disease (Excluding Essential Hypertension)	0.92 (0.76,1.11)	0.405
15-5	Myocardial Infarction	1.11 (0.88,1.40)	0.392
15-6	Stroke or Transient Ischemic Attack	1.09 (0.77,1.56)	0.625
15-8	Systolic Blood Pressure	0.94 (0.78,1.12)	0.477
15-10	Diastolic Blood Pressure	1.16 (0.88,1.53)	0.289
15-11	Heart Sounds	1.00 (0.75,1.33)	0.978
15-12	Overall ECG	0.86 (0.74,1.01)	0.066
15-13	ECG: RBBB	1.08 (0.72,1.61)	0.715

Table Ref.	Clinical Parameter	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
15-14	ECG: LBBB	1.28 (0.59,2.76)	0.538
15-15	ECG: Nonspecific ST- and T-wave Changes	0.95 (0.80,1.14)	0.600
15-16	ECG: Bradycardia	0.83 (0.56,1.24)	0.360
15-17	ECG: Tachycardia	2.60 (0.72,9.44)	0.147
15-18	ECG: Arrhythmia	0.63 (0.46,0.85)	0.001
15-19	ECG: Evidence of Prior Myocardial Infarction	1.01 (0.71,1.44)	0.965
15-20	Funduscopic Examination	1.07 (0.85,1.35)	0.546
15-21	Carotid Bruits	1.26 (0.69,2.31)	0.454
15-22	Radial Pulses	1.32 (0.97,1.79)	0.086
15-23	Femoral Pulses	0.75 (0.42,1.36)	0.327
15-24	Popliteal Pulses	0.81 (0.50,1.33)	0.395
15-25	Dorsalis Pedis Pulses	1.06 (0.82,1.37)	0.658
15-26	Posterior Tibial Pulses	1.26 (0.90,1.76)	0.179
15-27	Leg Pulses	1.07 (0.83,1.36)	0.609
15-28	Peripheral Pulses	1.21 (0.99,1.49)	0.065
15-30	Resting Pressure Index	1.05 (0.74,1.48)	0.804
15-32	Hyperemic Pressure Index (1 Minute Post-exercise)	1.03 (0.81,1.32)	0.798
15-34	Hyperemic Pressure Index (2 Minutes Post-exercise)	1.10 (0.76,1.57)	0.623
15-35	Intermittent Claudication and Vascular Insufficiency Index	1.16 (0.77,1.73)	0.490
16-13	RBC Morphology	0.95 (0.71,1.25)	0.689
16-16	Absolute Neutrophils (Bands) (Zero vs. Nonzero)	0.96 (0.80,1.16)	0.681
16-20	Absolute Eosinophils (Zero vs. Nonzero)	0.96 (0.75,1.23)	0.768
16-22	Absolute Basophils (Zero vs. Nonzero)	0.99 (0.86,1.15)	0.928
16-24	Fibrinogen	1.05 (0.79,1.39)	0.741
16-26	Erythrocyte Sedimentation Rate	0.99 (0.80,1.23)	0.934
17-3	Occurrence of Kidney Stones	0.72 (0.56,0.93)	0.008
17-4	Occurrence of Past Kidney Disease	1.02 (0.87,1.18)	0.844
17-9	Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero vs. Zero)	0.93 (0.76,1.15)	0.509
17-11	Urinary Occult Blood	0.72 (0.45,1.16)	0.157
17-12	Urinary WBC Count	0.95 (0.73,1.24)	0.699
17-13	Urinary Protein	0.98 (0.67,1.43)	0.901
18-3	Past Thyroid Disease	1.05 (0.82,1.33)	0.715
18-4	Composite Diabetes Indicator (2002 AFHS Diabetes Definition)	1.06 (0.88,1.27)	0.520
18-5	Composite Diabetes Indicator (Pre-2002 AFHS Diabetes Definition)	1.10 (0.92,1.31)	0.286
18-8	Time to Diabetes Onset (2002 AFHS Diabetes Definition)	1.04 (0.90,1.20)[c]	0.628[c]
18-9	Time to Diabetes Onset (Pre-2002 AFHS Diabetes Definition)	1.05 (0.91,1.20)[c]	0.542[c]
18-10	Thyroid Gland	0.30 (0.04,2.25)	0.134
18-11	Testicular Examination	1.12 (0.86,1.45)	0.413
18-15	Free T$_4$	0.98 (0.76,1.26)	0.857
18-16	Anti-thyroid Antibodies	0.75 (0.28,2.03)	0.548
18-18	Fasting Glucose	1.02 (0.86,1.22)	0.811
18-20	2-hour Postprandial Glucose (Nondiabetics Only)	0.79 (0.63,0.99)	0.037
18-21	2-hour Postprandial Urinary Glucose (Nondiabetics Only)	1.07 (0.88,1.30)	0.502
18-27	Hemoglobin A1c (Diabetics Only)	1.51 (1.05,2.19)	0.017
18-29	C-peptide (Diabetics Only)	0.73 (0.52,1.04)	0.068
18-31	Proinsulin (Diabetics Only)	0.86 (0.64,1.14)	0.288
18-32	GADA (Diabetics Only)	1.23 (0.58,2.59)	0.602
18-34	Total Testosterone	0.98 (0.81,1.18)	0.835
18-36	Free Testosterone	0.94 (0.70,1.27)	0.686

Table G-6. Summary of Unadjusted Results for Dichotomous Variables – Model 2 (Ranch Hands: Log$_2$ (Initial Dioxin)) (Continued)

Table Ref.	Clinical Parameter	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
18-38	Estradiol	1.52 (0.97,2.37)	0.073
18-40	LH	0.95 (0.66,1.37)	0.789
18-42	FSH	0.79 (0.56,1.12)	0.174
19-14	Lupus Panel: ANA Test	1.22 (1.01,1.47)	0.037
19-15	Lupus Panel: Thyroid Microsomal Antibody	0.99 (0.66,1.51)	0.979
19-16	Lupus Panel: MSK Antismooth Muscle Antibody	0.46 (0.14,1.56)	0.158
19-17	Lupus Panel: MSK Antimitochondrial Antibody	--	--
19-18	Lupus Panel: MSK Antiparietal Cell Antibody	1.18 (0.70,1.98)	0.536
19-19	Lupus Panel: Rheumatoid Factor	0.68 (0.56,0.84)	<0.001
20-3	Asthma	0.99 (0.72,1.37)	0.964
20-4	Bronchitis	1.01 (0.86,1.18)	0.907
20-5	Pneumonia	0.84 (0.67,1.06)	0.125
20-6	Thorax and Lung Abnormality	1.04 (0.88,1.24)	0.645
20-7	X-ray Interpretation	0.80 (0.64,1.00)	0.040
20-9	FVC	0.82 (0.64,1.05)	0.112
20-11	FEV$_1$	0.91 (0.78,1.06)	0.227

[a]Adjusted for body mass index at the time of the blood measurement for dioxin.
[b]Relative risk for a twofold increase in initial dioxin.
[c]Hazard ratio, confidence interval, and p-value, based on proportional hazards model, were given for time to diabetes onset variable.

--: Relative risk, confidence interval, and p-value were not presented because of the sparse number of Ranch Hands with abnormalities.

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
9-3	Self-perception of Health	Comparison	1,172	158 (13.5)		
		Background RH	352	41 (11.6)	0.90 (0.62,1.31)	0.592
		Low RH	211	29 (13.7)	1.00 (0.65,1.53)	0.999
		High RH	213	40 (18.8)	1.40 (0.95,2.06)	0.085
		Low plus High RH	424	69 (16.3)	1.19 (0.87,1.62)	0.285
9-4	Appearance of Illness or Distress	Comparison	1,174	50 (4.3)		
		Background RH	351	14 (4.0)	1.03 (0.56,1.90)	0.916
		Low RH	211	10 (4.7)	1.08 (0.53,2.16)	0.839
		High RH	213	7 (3.3)	0.70 (0.31,1.57)	0.381
		Low plus High RH	424	17 (4.0)	0.86 (0.49,1.53)	0.618
9-5	Relative Age Appearance	Comparison	1,174	48 (4.1)		
		Background RH	351	10 (2.8)	0.75 (0.38,1.51)	0.425
		Low RH	211	13 (6.2)	1.49 (0.79,2.81)	0.217
		High RH	213	18 (8.5)	2.01 (1.14,3.54)	0.016
		Low plus High RH	424	31 (7.3)	1.73 (1.08,2.78)	0.023
9-7	Body Mass Index	Comparison	1,174	415 (35.3)		
		Background RH	351	81 (23.1)	0.55 (0.42,0.72)	<0.001
		Low RH	211	93 (44.1)	1.44 (1.07,1.94)	0.016
		High RH	213	100 (46.9)	1.62 (1.21,2.17)	0.001
		Low plus High RH	424	193 (45.5)	1.53 (1.22,1.91)	<0.001
10-3	All Skin Neoplasms	Comparison	1,086	519 (47.8)		
		Background RH	331	179 (54.1)	1.31 (1.02,1.67)	0.035
		Low RH	187	114 (61.0)	1.69 (1.23,2.32)	0.001
		High RH	202	97 (48.0)	0.99 (0.73,1.34)	0.965
		Low plus High RH	389	211 (54.2)	1.28 (1.01,1.62)	0.037
10-4	Malignant Skin Neoplasms	Comparison	1,086	234 (21.5)		
		Background RH	331	86 (26.0)	1.30 (0.98,1.73)	0.073
		Low RH	187	59 (31.6)	1.66 (1.18,2.34)	0.004
		High RH	202	37 (18.3)	0.80 (0.54,1.18)	0.261
		Low plus High RH	389	96 (24.7)	1.14 (0.86,1.50)	0.365
10-5	Benign Skin Neoplasms	Comparison	1,161	397 (34.2)		
		Background RH	349	135 (38.7)	1.23 (0.96,1.58)	0.103
		Low RH	208	84 (40.4)	1.30 (0.96,1.76)	0.090
		High RH	212	76 (35.8)	1.06 (0.78,1.44)	0.699
		Low plus High RH	420	160 (38.1)	1.17 (0.93,1.48)	0.177
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	Comparison	1,086	5 (0.5)		
		Background RH	331	4 (1.2)	2.83 (0.75,10.71)	0.125
		Low RH	187	4 (2.1)	4.51 (1.19,17.06)	0.026
		High RH	202	0 (0.0)	--	0.726[c]
		Low plus High RH	389	4 (1.0)	--	0.393[c]

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
10-7	Basal Cell Carcinoma	Comparison	1,086	183 (16.9)		
		Background RH	331	75 (22.7)	1.47 (1.09,2.00)	0.012
		Low RH	187	50 (26.7)	1.78 (1.24,2.56)	0.002
		High RH	202	28 (13.9)	0.78 (0.50,1.20)	0.250
		Low plus High RH	389	78 (20.1)	1.16 (0.85,1.57)	0.349
10-8	Squamous Cell Carcinoma	Comparison	1,086	61 (5.6)		
		Background RH	331	20 (6.0)	1.09 (0.65,1.84)	0.750
		Low RH	187	15 (8.0)	1.46 (0.81,2.63)	0.208
		High RH	202	9 (4.5)	0.78 (0.38,1.59)	0.492
		Low plus High RH	389	24 (6.2)	1.05 (0.64,1.74)	0.844
10-9	Nonmelanoma	Comparison	1,086	213 (19.6)		
		Background RH	331	84 (25.4)	1.42 (1.06,1.90)	0.018
		Low RH	187	56 (29.9)	1.73 (1.22,2.45)	0.002
		High RH	202	34 (16.8)	0.81 (0.54,1.21)	0.306
		Low plus High RH	389	90 (23.1)	1.17 (0.88,1.56)	0.287
10-10	Melanoma	Comparison	1,086	31 (2.9)		
		Background RH	331	8 (2.4)	0.85 (0.38,1.87)	0.682
		Low RH	187	7 (3.7)	1.32 (0.57,3.04)	0.517
		High RH	202	4 (2.0)	0.68 (0.24,1.96)	0.479
		Low plus High RH	389	11 (2.8)	0.94 (0.45,1.94)	0.861
10-11	Systemic Neoplasms	Comparison	1,170	389 (33.2)		
		Background RH	350	114 (32.6)	1.00 (0.77,1.29)	0.993
		Low RH	204	84 (41.2)	1.39 (1.03,1.89)	0.033
		High RH	210	64 (30.5)	0.86 (0.62,1.18)	0.345
		Low plus High RH	414	148 (35.7)	1.09 (0.86,1.38)	0.482
10-12	Malignant Systemic Neoplasms	Comparison	1,172	118 (10.1)		
		Background RH	350	40 (11.4)	1.16 (0.79,1.70)	0.444
		Low RH	206	40 (19.4)	2.15 (1.45,3.19)	<0.001
		High RH	212	17 (8.0)	0.77 (0.45,1.32)	0.345
		Low plus High RH	418	57 (13.6)	1.28 (0.89,1.83)	0.179
10-13	Benign Systemic Neoplasms	Comparison	1,170	294 (25.1)		
		Background RH	350	87 (24.9)	1.02 (0.77,1.34)	0.915
		Low RH	204	53 (26.0)	1.04 (0.74,1.45)	0.842
		High RH	210	52 (24.8)	0.96 (0.68,1.34)	0.793
		Low plus High RH	414	105 (25.4)	0.99 (0.77,1.29)	0.963
10-14	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	Comparison	1,172	25 (2.1)		
		Background RH	350	8 (2.3)	1.14 (0.50,2.56)	0.757
		Low RH	206	5 (2.4)	1.12 (0.42,2.95)	0.826
		High RH	212	2 (0.9)	0.42 (0.10,1.77)	0.236
		Low plus High RH	418	7 (1.7)	0.68 (0.27,1.70)	0.406
10-16	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	Comparison	1,172	4 (0.3)		
		Background RH	350	0 (0.0)	--	0.617[c]
		Low RH	206	0 (0.0)	--	0.891[c]
		High RH	212	1 (0.5)	1.32 (0.14,12.02)	0.806
		Low plus High RH	418	1 (0.2)	--	0.999[c]

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
10-17	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	Comparison	1,172	9	(0.8)		
		Background RH	350	0	(0.0)	--	0.212[c]
		Low RH	206	4	(1.9)	2.62 (0.80,8.60)	0.112
		High RH	212	0	(0.0)	--	0.415[c]
		Low plus High RH	418	4	(1.0)	--	0.958[c]
10-18	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	Comparison	1,172	1	(0.1)		
		Background RH	350	2	(0.6)	6.35 (0.56,72.10)	0.136
		Low RH	206	0	(0.0)	--	0.999[c]
		High RH	212	0	(0.0)	--	0.999[c]
		Low plus High RH	418	0	(0.0)	--	0.999[c]
10-19	Malignant Systemic Neoplasms (Thyroid Gland)	Comparison	1,172	2	(0.2)		
		Background RH	350	0	(0.0)	--	0.999[c]
		Low RH	206	1	(0.5)	2.97 (0.27,33.03)	0.375
		High RH	212	0	(0.0)	--	0.999[c]
		Low plus High RH	418	1	(0.2)	--	0.999[c]
10-20	Malignant Systemic Neoplasms (Bronchus and Lung)	Comparison	1,172	7	(0.6)		
		Background RH	350	3	(0.9)	1.60 (0.41,6.26)	0.500
		Low RH	206	8	(3.9)	6.43 (2.30,18.02)	<0.001
		High RH	212	2	(0.9)	1.44 (0.30,7.04)	0.650
		Low plus High RH	418	10	(2.4)	3.01 (1.02,8.95)	0.047
10-21	All Stomach Neoplasms	Comparison	1,172	8	(0.7)		
		Background RH	350	3	(0.9)	1.27 (0.33,4.86)	0.727
		Low RH	206	2	(1.0)	1.42 (0.30,6.75)	0.658
		High RH	212	1	(0.5)	0.68 (0.08,5.52)	0.721
		Low plus High RH	418	3	(0.7)	0.98 (0.24,3.97)	0.978
10-22	Malignant Systemic Neoplasms (Colon and Rectum)	Comparison	1,172	10	(0.9)		
		Background RH	350	3	(0.9)	1.20 (0.33,4.42)	0.784
		Low RH	206	7	(3.4)	3.74 (1.39,10.07)	0.009
		High RH	212	2	(0.9)	0.93 (0.20,4.34)	0.927
		Low plus High RH	418	9	(2.2)	1.85 (0.66,5.14)	0.240
10-23	Malignant Systemic Neoplasms (Urinary System)	Comparison	1,172	12	(1.0)		
		Background RH	350	9	(2.6)	2.77 (1.15,6.68)	0.023
		Low RH	206	6	(2.9)	2.80 (1.04,7.58)	0.042
		High RH	212	3	(1.4)	1.29 (0.36,4.64)	0.694
		Low plus High RH	418	9	(2.2)	1.89 (0.76,4.70)	0.169
10-24	Malignant Systemic Neoplasms (Kidney and Ureter)	Comparison	1,172	4	(0.3)		
		Background RH	350	4	(1.1)	3.70 (0.91,15.08)	0.068
		Low RH	206	2	(1.0)	2.75 (0.50,15.16)	0.247
		High RH	212	1	(0.5)	1.28 (0.14,11.56)	0.829
		Low plus High RH	418	3	(0.7)	1.86 (0.39,8.91)	0.437

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
10-25	Malignant Systemic Neoplasms (Prostate)	Comparison	1,172	67	(5.7)		
		Background RH	350	22	(6.3)	1.06 (0.64,1.74)	0.834
		Low RH	206	22	(10.7)	2.00 (1.21,3.32)	0.007
		High RH	212	9	(4.2)	0.76 (0.37,1.55)	0.454
		Low plus High RH	418	31	(7.4)	1.23 (0.76,1.97)	0.399
10-26	Malignant Systemic Neoplasms (Penis and Other Male Genital Organs)	Comparison	1,172	0	(0.0)		
		Background RH	350	0	(0.0)	--	--
		Low RH	206	0	(0.0)	--	--
		High RH	212	2	(0.9)	--	0.019[c]
		Low plus High RH	418	2	(0.5)	--	0.117[c]
10-27	Malignant Systemic Neoplasms (Testicles)	Comparison	1,172	0	(0.0)		
		Background RH	350	0	(0.0)	--	--
		Low RH	206	2	(1.0)	--	0.017[c]
		High RH	212	1	(0.5)	--	0.335[c]
		Low plus High RH	418	3	(0.7)	--	0.025[c]
10-28	Malignant Systemic Neoplasms (Bone and Articular Cartilage)	Comparison	1,172	4	(0.3)		
		Background RH	350	0	(0.0)	--	0.617[c]
		Low RH	206	0	(0.0)	--	0.891[c]
		High RH	212	0	(0.0)	--	0.876[c]
		Low plus High RH	418	0	(0.0)	--	0.531[c]
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	Comparison	1,172	6	(0.5)		
		Background RH	350	0	(0.0)	--	0.392[c]
		Low RH	206	0	(0.0)	--	0.649[c]
		High RH	212	1	(0.5)	0.82 (0.10,6.98)	0.858
		Low plus High RH	418	1	(0.2)	--	0.770[c]
10-30	Carcinoma in Situ	Comparison	1,172	6	(0.5)		
		Background RH	350	1	(0.3)	0.56 (0.07,4.71)	0.594
		Low RH	206	3	(1.5)	2.87 (0.71,11.57)	0.139
		High RH	212	0	(0.0)	--	0.634[c]
		Low plus High RH	418	3	(0.7)	--	0.919[c]
10-31	Hodgkin's Disease	Comparison	1,172	1	(0.1)		
		Background RH	350	1	(0.3)	3.14 (0.19,52.10)	0.424
		Low RH	206	0	(0.0)	--	0.999[c]
		High RH	212	0	(0.0)	--	0.999[c]
		Low plus High RH	418	0	(0.0)	--	0.999[c]
10-32	Leukemia	Comparison	1,172	6	(0.5)		
		Background RH	350	4	(1.1)	2.06 (0.57,7.44)	0.271
		Low RH	206	0	(0.0)	--	0.649[c]
		High RH	212	0	(0.0)	--	0.634[c]
		Low plus High RH	418	0	(0.0)	--	0.317[c]

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
10-33	Other Malignant Systemic Neoplasms (Lymphoid and Histiocytic Tissue)	Comparison	1,172	9 (0.8)		
		Background RH	350	1 (0.3)	0.39 (0.05,3.12)	0.377
		Low RH	206	4 (1.9)	2.50 (0.76,8.22)	0.131
		High RH	212	1 (0.5)	0.58 (0.07,4.64)	0.610
		Low plus High RH	418	5 (1.2)	1.19 (0.33,4.35)	0.788
10-34	Lymphoreticular Sarcoma	Comparison	1,172	3 (0.3)		
		Background RH	350	1 (0.3)	0.91 (0.09,8.96)	0.939
		Low RH	206	0 (0.0)	--	0.999[c]
		High RH	212	0 (0.0)	--	0.999[c]
		Low plus High RH	418	0 (0.0)	--	0.705[c]
10-35	Skin and Systemic Neoplasms	Comparison	1,157	714 (61.7)		
		Background RH	347	229 (66.0)	1.22 (0.95,1.57)	0.123
		Low RH	202	149 (73.8)	1.74 (1.24,2.43)	0.001
		High RH	209	124 (59.3)	0.89 (0.66,1.21)	0.467
		Low plus High RH	411	273 (66.4)	1.24 (0.97,1.58)	0.080
10-36	Malignant Skin and Systemic Neoplasms	Comparison	1,159	318 (27.4)		
		Background RH	347	110 (31.7)	1.24 (0.95,1.57)	0.113
		Low RH	203	84 (41.4)	1.86 (1.37,2.53)	<0.001
		High RH	211	46 (21.8)	0.73 (0.52,1.04)	0.084
		Low plus High RH	414	130 (31.4)	1.16 (0.90,1.49)	0.255
10-38	PSA	Comparison	1,089	58 (5.3)		
		Background RH	325	15 (4.6)	0.84 (0.47,1.51)	0.566
		Low RH	187	12 (6.4)	1.23 (0.64,2.33)	0.534
		High RH	201	5 (2.5)	0.46 (0.18,1.17)	0.103
		Low plus High RH	388	17 (4.4)	0.74 (0.40,1.35)	0.326
11-3	Inflammatory Diseases	Comparison	1,161	7 (0.6)		
		Background RH	352	5 (1.4)	2.23 (0.70,7.15)	0.176
		Low RH	211	2 (0.9)	1.60 (0.33,7.76)	0.560
		High RH	210	2 (1.0)	1.68 (0.34,8.18)	0.523
		Low plus High RH	421	4 (1.0)	1.64 (0.48,5.64)	0.435
11-4	Hereditary and Degenerative Diseases	Comparison	1,169	163 (13.9)		
		Background RH	352	59 (16.8)	1.26 (0.91,1.75)	0.168
		Low RH	211	35 (16.6)	1.22 (0.82,1.82)	0.323
		High RH	210	34 (16.2)	1.18 (0.79,1.77)	0.426
		Low plus High RH	421	69 (16.4)	1.20 (0.88,1.63)	0.244
11-5	Peripheral Disorders	Comparison	1,166	305 (26.2)		
		Background RH	350	87 (24.9)	1.02 (0.77,1.35)	0.874
		Low RH	211	65 (30.8)	1.23 (0.89,1.70)	0.214
		High RH	210	59 (28.1)	1.02 (0.73,1.42)	0.920
		Low plus High RH	421	124 (29.5)	1.12 (0.87,1.44)	0.383

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
11-6	Other Neurological Disorders	Comparison	1,166	198 (17.0)		
		Background RH	350	52 (14.9)	0.83 (0.59,1.16)	0.274
		Low RH	211	47 (22.3)	1.41 (0.99,2.02)	0.060
		High RH	210	52 (24.8)	1.65 (1.16,2.34)	0.005
		Low plus High RH	421	99 (23.5)	1.53 (1.16,2.01)	0.002
11-7	Smell	Comparison	1,168	27 (2.3)		
		Background RH	351	13 (3.7)	1.72 (0.87,3.39)	0.119
		Low RH	211	8 (3.8)	1.64 (0.73,3.66)	0.230
		High RH	210	0 (0.0)	--	0.051[c]
		Low plus High RH	421	8 (1.9)	--	0.765[c]
11-8	Visual Fields	Comparison	1,157	7 (0.6)		
		Background RH	350	8 (2.3)	4.37 (1.55,12.30)	0.005
		Low RH	209	2 (1.0)	1.51 (0.31,7.34)	0.613
		High RH	209	2 (1.0)	1.41 (0.29,6.91)	0.671
		Low plus High RH	418	4 (1.0)	1.46 (0.42,5.05)	0.552
11-9	Light Reaction	Comparison	1,165	8 (0.7)		
		Background RH	350	3 (0.9)	1.12 (0.29,4.31)	0.865
		Low RH	211	0 (0.0)	--	0.475[c]
		High RH	210	1 (0.5)	0.76 (0.09,6.18)	0.800
		Low plus High RH	421	1 (0.2)	--	0.501[c]
11-10	Ocular Movement	Comparison	1,166	4 (0.3)		
		Background RH	350	3 (0.9)	2.69 (0.59,12.28)	0.201
		Low RH	211	1 (0.5)	1.35 (0.15,12.16)	0.789
		High RH	210	1 (0.5)	1.31 (0.14,11.85)	0.813
		Low plus High RH	421	2 (0.5)	1.33 (0.24,7.32)	0.745
11-11	Facial Sensation	Comparison	1,169	3 (0.3)		
		Background RH	351	1 (0.3)	0.99 (0.10,9.64)	0.993
		Low RH	211	3 (1.4)	5.74 (1.15,28.69)	0.033
		High RH	210	0 (0.0)	--	0.999[c]
		Low plus High RH	421	3 (0.7)	--	0.398[c]
11-12	Corneal Reflex	Comparison	1,162	5 (0.4)		
		Background RH	350	1 (0.3)	0.56 (0.06,4.86)	0.598
		Low RH	211	0 (0.0)	--	0.739[c]
		High RH	210	1 (0.5)	1.30 (0.15,11.38)	0.811
		Low plus High RH	421	1 (0.2)	--	0.929[c]
11-13	Smile	Comparison	1,169	11 (0.9)		
		Background RH	351	2 (0.6)	0.70 (0.15,3.20)	0.647
		Low RH	211	4 (1.9)	1.90 (0.59,6.07)	0.281
		High RH	210	2 (1.0)	0.87 (0.19,4.02)	0.862
		Low plus High RH	421	6 (1.4)	1.29 (0.45,3.68)	0.636
11-14	Palpebral Fissure	Comparison	1,168	23 (2.0)		
		Background RH	351	11 (3.1)	1.66 (0.79,3.45)	0.179
		Low RH	211	7 (3.3)	1.69 (0.72,4.00)	0.229
		High RH	210	5 (2.4)	1.19 (0.44,3.17)	0.734
		Low plus High RH	421	12 (2.9)	1.42 (0.69,2.90)	0.339

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
11-15	Balance	Comparison	1,168	22 (1.9)		
		Background RH	350	7 (2.0)	1.07 (0.45,2.53)	0.886
		Low RH	211	6 (2.8)	1.52 (0.61,3.81)	0.367
		High RH	210	5 (2.4)	1.27 (0.47,3.40)	0.637
		Low plus High RH	421	11 (2.6)	1.39 (0.67,2.90)	0.380
11-16	Gag Reflex	Comparison	1,169	1 (0.1)		
		Background RH	351	0 (0.0)	--	0.999[c]
		Low RH	211	1 (0.5)	5.77 (0.36,93.26)	0.217
		High RH	210	1 (0.5)	7.61 (0.46,126.82)	0.158
		Low plus High RH	421	2 (0.5)	6.62 (0.59,74.18)	0.125
11-17	Speech	Comparison	1,169	12 (1.0)		
		Background RH	351	5 (1.4)	1.47 (0.51,4.25)	0.473
		Low RH	211	2 (0.9)	0.91 (0.20,4.08)	0.897
		High RH	210	3 (1.4)	1.33 (0.37,4.78)	0.663
		Low plus High RH	421	5 (1.2)	1.10 (0.38,3.19)	0.866
11-18	Tongue Position Relative to Midline	Comparison	1,169	2 (0.2)		
		Background RH	351	0 (0.0)	--	0.999[c]
		Low RH	211	2 (0.9)	5.55 (0.78,39.71)	0.088
		High RH	210	1 (0.5)	2.75 (0.25,30.77)	0.413
		Low plus High RH	421	3 (0.7)	3.91 (0.62,24.68)	0.147
11-19	Shoulder Shrug	Comparison	1,169	6 (0.5)		
		Background RH	351	1 (0.3)	0.64 (0.08,5.35)	0.677
		Low RH	211	2 (0.9)	1.74 (0.35,8.76)	0.502
		High RH	210	0 (0.0)	--	0.638[c]
		Low plus High RH	421	2 (0.5)	--	0.999[c]
11-20	Cranial Nerve Index	Comparison	1,157	89 (7.7)		
		Background RH	348	40 (11.5)	1.61 (1.08,2.39)	0.019
		Low RH	209	26 (12.4)	1.69 (1.06,2.69)	0.027
		High RH	210	16 (7.6)	0.96 (0.55,1.68)	0.895
		Low plus High RH	419	42 (10.0)	1.28 (0.86,1.89)	0.226
11-21	Pinprick	Comparison	984	88 (8.9)		
		Background RH	303	28 (9.2)	1.11 (0.71,1.75)	0.640
		Low RH	163	14 (8.6)	0.95 (0.53,1.71)	0.862
		High RH	170	26 (15.3)	1.76 (1.09,2.82)	0.020
		Low plus High RH	333	40 (12.0)	1.30 (0.86,1.95)	0.208
11-22	Light Touch	Comparison	984	56 (5.7)		
		Background RH	303	15 (5.0)	0.91 (0.50,1.64)	0.754
		Low RH	163	9 (5.5)	0.96 (0.47,1.99)	0.919
		High RH	170	16 (9.4)	1.66 (0.93,2.98)	0.088
		Low plus High RH	333	25 (7.5)	1.27 (0.77,2.10)	0.346
11-23	Muscle Status	Comparison	1,168	58 (5.0)		
		Background RH	347	18 (5.2)	1.02 (0.59,1.77)	0.936
		Low RH	211	12 (5.7)	1.16 (0.61,2.20)	0.648
		High RH	209	12 (5.7)	1.19 (0.63,2.26)	0.598
		Low plus High RH	420	24 (5.7)	1.17 (0.72,1.92)	0.520

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
11-27	Babinski Reflex	Comparison	1,165	18 (1.5)		
		Background RH	350	5 (1.4)	1.07 (0.39,2.93)	0.893
		Low RH	211	3 (1.4)	0.86 (0.25,2.96)	0.806
		High RH	210	2 (1.0)	0.53 (0.12,2.33)	0.401
		Low plus High RH	421	5 (1.2)	0.67 (0.24,1.87)	0.450
11-28	Any Symmetric Peripheral Abnormality	Comparison	1,130	249 (22.0)		
		Background RH	337	68 (20.2)	1.03 (0.76,1.41)	0.834
		Low RH	209	62 (29.7)	1.46 (1.04,2.04)	0.027
		High RH	203	54 (26.6)	1.14 (0.80,1.61)	0.478
		Low plus High RH	412	116 (28.2)	1.29 (0.99,1.68)	0.058
11-29	Possible Peripheral Neuropathy	Comparison	1,131	242 (21.4)		
		Background RH	337	64 (19.0)	1.00 (0.73,1.37)	0.990
		Low RH	209	60 (28.7)	1.45 (1.03,2.03)	0.034
		High RH	203	50 (24.6)	1.05 (0.73,1.51)	0.780
		Low plus High RH	412	110 (26.7)	1.24 (0.95,1.62)	0.120
11-30	Probable Peripheral Neuropathy	Comparison	1,131	79 (7.0)		
		Background RH	337	25 (7.4)	1.24 (0.77,1.99)	0.376
		Low RH	209	18 (8.6)	1.19 (0.69,2.05)	0.525
		High RH	202	19 (9.4)	1.22 (0.71,2.08)	0.468
		Low plus High RH	411	37 (9.0)	1.21 (0.80,1.83)	0.378
11-31	Tremor	Comparison	1,169	86 (7.4)		
		Background RH	351	24 (6.8)	0.94 (0.59,1.51)	0.795
		Low RH	211	10 (4.7)	0.62 (0.32,1.22)	0.168
		High RH	210	20 (9.5)	1.31 (0.78,2.18)	0.306
		Low plus High RH	421	30 (7.1)	0.90 (0.57,1.42)	0.654
11-32	Coordination	Comparison	1,168	61 (5.2)		
		Background RH	350	16 (4.6)	0.88 (0.50,1.55)	0.650
		Low RH	210	6 (2.9)	0.53 (0.23,1.25)	0.147
		High RH	209	9 (4.3)	0.81 (0.40,1.66)	0.567
		Low plus High RH	419	15 (3.6)	0.66 (0.37,1.18)	0.160
11-33	Romberg Sign	Comparison	1,168	22 (1.9)		
		Background RH	350	7 (2.0)	1.07 (0.45,2.53)	0.886
		Low RH	211	6 (2.8)	1.52 (0.61,3.81)	0.367
		High RH	210	5 (2.4)	1.27 (0.47,3.40)	0.637
		Low plus High RH	421	11 (2.6)	1.39 (0.67,2.90)	0.380
11-34	Gait	Comparison	1,169	98 (8.4)		
		Background RH	351	23 (6.6)	0.85 (0.53,1.36)	0.487
		Low RH	211	20 (9.5)	1.11 (0.66,1.84)	0.699
		High RH	210	22 (10.5)	1.17 (0.72,1.92)	0.526
		Low plus High RH	421	42 (10.0)	1.14 (0.78,1.67)	0.507
11-35	CNS Index	Comparison	1,169	183 (15.7)		
		Background RH	351	47 (13.4)	0.89 (0.63,1.25)	0.495
		Low RH	211	29 (13.7)	0.84 (0.55,1.29)	0.424
		High RH	210	37 (17.6)	1.09 (0.74,1.61)	0.661
		Low plus High RH	421	66 (15.7)	0.96 (0.70,1.31)	0.785

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
12-3	Psychoses	Comparison	1,172	74 (6.3)		
		Background RH	352	18 (5.1)	0.81 (0.48,1.38)	0.436
		Low RH	211	12 (5.7)	0.89 (0.48,1.67)	0.721
		High RH	210	16 (7.6)	1.21 (0.69,2.13)	0.506
		Low plus High RH	421	28 (6.7)	1.04 (0.66,1.64)	0.870
12-4	Alcohol Dependence	Comparison	1,171	66 (5.6)		
		Background RH	352	22 (6.3)	1.09 (0.66,1.79)	0.748
		Low RH	211	10 (4.7)	0.84 (0.42,1.66)	0.613
		High RH	210	14 (6.7)	1.23 (0.67,2.23)	0.505
		Low plus High RH	421	24 (5.7)	1.01 (0.62,1.65)	0.957
12-5	Drug Dependence	Comparison	1,172	5 (0.4)		
		Background RH	352	2 (0.6)	0.99 (0.19,5.19)	0.990
		Low RH	211	0 (0.0)	--	0.743[c]
		High RH	210	0 (0.0)	--	0.746[c]
		Low plus High RH	421	0 (0.0)	--	0.404[c]
12-6	Anxiety	Comparison	1,169	331 (28.3)		
		Background RH	350	89 (25.4)	0.87 (0.66,1.14)	0.314
		Low RH	211	63 (29.9)	1.08 (0.78,1.48)	0.656
		High RH	209	73 (34.9)	1.35 (0.99,1.85)	0.059
		Low plus High RH	420	136 (32.4)	1.21 (0.95,1.53)	0.131
12-7	Other Neuroses	Comparison	1,162	692 (59.6)		
		Background RH	346	179 (51.7)	0.75 (0.59,0.95)	0.020
		Low RH	211	132 (62.6)	1.13 (0.83,1.53)	0.439
		High RH	208	142 (68.3)	1.43 (1.04,1.96)	0.028
		Low plus High RH	419	274 (65.4)	1.27 (1.00,1.60)	0.048
12-8	SCL-90-R Anxiety	Comparison	1,171	106 (9.1)		
		Background RH	351	20 (5.7)	0.62 (0.38,1.01)	0.056
		Low RH	210	19 (9.0)	0.99 (0.60,1.66)	0.983
		High RH	210	25 (11.9)	1.34 (0.84,2.13)	0.220
		Low plus High RH	420	44 (10.5)	1.15 (0.79,1.68)	0.454
12-9	SCL-90-R Depression	Comparison	1,171	143 (12.2)		
		Background RH	351	31 (8.8)	0.73 (0.48,1.09)	0.126
		Low RH	210	21 (10.0)	0.79 (0.49,1.28)	0.335
		High RH	210	33 (15.7)	1.29 (0.85,1.95)	0.225
		Low plus High RH	420	54 (12.9)	1.01 (0.72,1.42)	0.960
12-10	SCL-90-R Hostility	Comparison	1,171	65 (5.6)		
		Background RH	351	17 (4.8)	0.89 (0.51,1.54)	0.664
		Low RH	210	5 (2.4)	0.41 (0.16,1.04)	0.060
		High RH	210	19 (9.0)	1.66 (0.97,2.84)	0.064
		Low plus High RH	420	24 (5.7)	0.83 (0.47,1.45)	0.509
12-11	SCL-90-R Interpersonal Sensitivity	Comparison	1,171	125 (10.7)		
		Background RH	351	24 (6.8)	0.61 (0.39,0.96)	0.034
		Low RH	210	10 (4.8)	0.42 (0.22,0.81)	0.010
		High RH	210	23 (11.0)	1.04 (0.65,1.66)	0.884
		Low plus High RH	420	33 (7.9)	0.66 (0.43,1.01)	0.056

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
12-12	SCL-90-R Obsessive-compulsive Behavior	Comparison	1,171	212 (18.1)		
		Background RH	351	50 (14.2)	0.78 (0.56,1.09)	0.151
		Low RH	210	28 (13.3)	0.69 (0.45,1.05)	0.084
		High RH	210	46 (21.9)	1.23 (0.85,1.76)	0.270
		Low plus High RH	420	74 (17.6)	0.92 (0.68,1.24)	0.571
12-13	SCL-90-R Paranoid Ideation	Comparison	1,171	65 (5.6)		
		Background RH	351	10 (2.8)	0.51 (0.26,1.01)	0.052
		Low RH	210	4 (1.9)	0.33 (0.12,0.91)	0.032
		High RH	210	10 (4.8)	0.83 (0.42,1.66)	0.605
		Low plus High RH	420	14 (3.3)	0.52 (0.28,0.99)	0.047
12-14	SCL-90-R Phobic Anxiety	Comparison	1,171	100 (8.5)		
		Background RH	351	25 (7.1)	0.85 (0.54,1.34)	0.487
		Low RH	210	12 (5.7)	0.64 (0.35,1.19)	0.160
		High RH	210	18 (8.6)	0.97 (0.57,1.65)	0.920
		Low plus High RH	420	30 (7.1)	0.79 (0.51,1.22)	0.286
12-15	SCL-90-R Psychoticism	Comparison	1,171	123 (10.5)		
		Background RH	351	27 (7.7)	0.74 (0.48,1.15)	0.183
		Low RH	210	12 (5.7)	0.51 (0.28,0.94)	0.030
		High RH	210	29 (13.8)	1.31 (0.85,2.03)	0.224
		Low plus High RH	420	41 (9.8)	0.82 (0.55,1.22)	0.320
12-16	SCL-90-R Somatization	Comparison	1,171	172 (14.7)		
		Background RH	351	40 (11.4)	0.81 (0.56,1.17)	0.253
		Low RH	210	21 (10.0)	0.63 (0.39,1.01)	0.057
		High RH	210	42 (20.0)	1.36 (0.93,1.99)	0.111
		Low plus High RH	420	63 (15.0)	0.92 (0.67,1.28)	0.630
12-17	SCL-90-R Global Severity Index	Comparison	1,171	143 (12.2)		
		Background RH	351	29 (8.3)	0.68 (0.45,1.04)	0.076
		Low RH	210	18 (8.6)	0.66 (0.39,1.11)	0.115
		High RH	210	33 (15.7)	1.28 (0.84,1.93)	0.246
		Low plus High RH	420	51 (12.1)	0.92 (0.65,1.31)	0.639
12-18	SCL-90-R Positive Symptom Total	Comparison	1,171	147 (12.6)		
		Background RH	351	30 (8.5)	0.68 (0.45,1.03)	0.071
		Low RH	210	14 (6.7)	0.49 (0.28,0.86)	0.014
		High RH	210	30 (14.3)	1.11 (0.73,1.70)	0.624
		Low plus High RH	420	44 (10.5)	0.74 (0.51,1.08)	0.113
12-19	SCL-90-R Positive Symptom Distress Index	Comparison	1,171	96 (8.2)		
		Background RH	351	18 (5.1)	0.64 (0.38,1.08)	0.096
		Low RH	210	15 (7.1)	0.84 (0.48,1.49)	0.556
		High RH	210	21 (10.0)	1.18 (0.72,1.95)	0.517
		Low plus High RH	420	36 (8.6)	1.00 (0.66,1.50)	0.991
13-3	Uncharacterized Hepatitis	Comparison	1,168	15 (1.3)		
		Background RH	349	5 (1.4)	1.17 (0.42,3.25)	0.769
		Low RH	210	3 (1.4)	1.10 (0.32,3.83)	0.883
		High RH	211	7 (3.3)	2.54 (1.02,6.35)	0.045
		Low plus High RH	421	10 (2.4)	1.67 (0.71,3.93)	0.238

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
13-4	Jaundice	Comparison	1,146	33	(2.9)		
		Background RH	340	11	(3.2)	1.09 (0.54,2.20)	0.803
		Low RH	207	2	(1.0)	0.33 (0.08,1.39)	0.131
		High RH	208	1	(0.5)	0.17 (0.02,1.23)	0.079
		Low plus High RH	415	3	(0.7)	0.24 (0.07,0.82)	0.024
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	Comparison	1,112	45	(4.0)		
		Background RH	333	16	(4.8)	1.24 (0.69,2.22)	0.481
		Low RH	201	5	(2.5)	0.60 (0.23,1.52)	0.280
		High RH	193	12	(6.2)	1.52 (0.79,2.95)	0.211
		Low plus High RH	394	17	(4.3)	0.94 (0.51,1.75)	0.855
13-6	Chronic Liver Disease and Cirrhosis (Nonalcohol-related)	Comparison	1,174	27	(2.3)		
		Background RH	352	8	(2.3)	1.17 (0.52,2.62)	0.705
		Low RH	211	9	(4.3)	1.76 (0.81,3.83)	0.156
		High RH	213	10	(4.7)	1.80 (0.85,3.83)	0.124
		Low plus High RH	424	19	(4.5)	1.78 (0.97,3.27)	0.063
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	Comparison	1,174	2	(0.2)		
		Background RH	352	2	(0.6)	3.18 (0.44,22.96)	0.251
		Low RH	211	1	(0.5)	2.83 (0.25,31.33)	0.397
		High RH	213	2	(0.9)	5.81 (0.81,41.95)	0.081
		Low plus High RH	424	3	(0.7)	4.06 (0.64,25.57)	0.136
13-8	Enlarged Liver	Comparison	1,173	45	(3.8)		
		Background RH	352	12	(3.4)	0.95 (0.49,1.82)	0.872
		Low RH	211	7	(3.3)	0.84 (0.37,1.89)	0.671
		High RH	212	8	(3.8)	0.93 (0.43,2.00)	0.844
		Low plus High RH	423	15	(3.5)	0.88 (0.48,1.60)	0.678
13-9	Other Disorders of the Liver	Comparison	1,165	527	(45.2)		
		Background RH	349	155	(44.4)	1.04 (0.81,1.33)	0.761
		Low RH	211	103	(48.8)	1.14 (0.84,1.53)	0.400
		High RH	213	107	(50.2)	1.15 (0.86,1.55)	0.345
		Low plus High RH	424	210	(49.5)	1.14 (0.91,1.43)	0.240
13-10	Current Hepatomegaly	Comparison	1,155	13	(1.1)		
		Background RH	348	5	(1.4)	1.42 (0.50,4.06)	0.508
		Low RH	209	5	(2.4)	2.06 (0.72,5.87)	0.175
		High RH	212	2	(0.9)	0.76 (0.17,3.41)	0.720
		Low plus High RH	421	7	(1.7)	1.25 (0.46,3.38)	0.664
13-12	AST	Comparison	1,154	83	(7.2)		
		Background RH	348	31	(8.9)	1.30 (0.84,2.01)	0.234
		Low RH	208	17	(8.2)	1.14 (0.66,1.96)	0.643
		High RH	211	17	(8.1)	1.10 (0.64,1.90)	0.732
		Low plus High RH	419	34	(8.1)	1.12 (0.74,1.70)	0.599
13-14	ALT	Comparison	1,154	88	(7.6)		
		Background RH	348	19	(5.5)	0.70 (0.42,1.17)	0.169
		Low RH	208	19	(9.1)	1.22 (0.72,2.05)	0.456
		High RH	211	16	(7.6)	1.00 (0.57,1.74)	0.990
		Low plus High RH	419	35	(8.4)	1.10 (0.73,1.66)	0.646

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
13-16	GGT	Comparison	1,154	127 (11.0)		
		Background RH	348	29 (8.3)	0.75 (0.49,1.15)	0.194
		Low RH	208	27 (13.0)	1.20 (0.77,1.87)	0.429
		High RH	211	21 (10.0)	0.87 (0.54,1.42)	0.588
		Low plus High RH	419	48 (11.5)	1.02 (0.72,1.46)	0.907
13-18	Alkaline Phosphatase	Comparison	1,154	70 (6.1)		
		Background RH	348	28 (8.0)	1.31 (0.83,2.08)	0.247
		Low RH	208	15 (7.2)	1.21 (0.68,2.17)	0.511
		High RH	211	20 (9.5)	1.67 (0.99,2.81)	0.055
		Low plus High RH	419	35 (8.4)	1.43 (0.93,2.18)	0.103
13-20	Total Bilirubin	Comparison	1,154	76 (6.6)		
		Background RH	348	23 (6.6)	1.01 (0.62,1.65)	0.957
		Low RH	208	17 (8.2)	1.26 (0.73,2.18)	0.410
		High RH	211	10 (4.7)	0.70 (0.36,1.38)	0.302
		Low plus High RH	419	27 (6.4)	0.94 (0.59,1.49)	0.784
13-21	Direct Bilirubin	Comparison	1,154	11 (1.0)		
		Background RH	348	2 (0.6)	0.69 (0.15,3.17)	0.635
		Low RH	208	0 (0.0)	--	0.321[c]
		High RH	211	0 (0.0)	--	0.315[c]
		Low plus High RH	419	0 (0.0)	--	0.096[c]
13-23	LDH	Comparison	1,154	108 (9.4)		
		Background RH	348	40 (11.5)	1.40 (0.95,2.07)	0.088
		Low RH	208	27 (13.0)	1.40 (0.89,2.20)	0.150
		High RH	211	18 (8.5)	0.82 (0.48,1.39)	0.458
		Low plus High RH	419	45 (10.7)	1.07 (0.73,1.56)	0.735
13-25	Cholesterol	Comparison	1,154	154 (13.3)		
		Background RH	348	40 (11.5)	0.78 (0.53,1.13)	0.184
		Low RH	208	20 (9.6)	0.70 (0.43,1.15)	0.160
		High RH	211	23 (10.9)	0.85 (0.53,1.36)	0.502
		Low plus High RH	419	43 (10.3)	0.77 (0.54,1.11)	0.164
13-27	HDL Cholesterol	Comparison	1,154	173 (15.0)		
		Background RH	348	57 (16.4)	1.26 (0.91,1.76)	0.167
		Low RH	208	37 (17.8)	1.18 (0.79,1.76)	0.414
		High RH	211	45 (21.3)	1.39 (0.96,2.03)	0.081
		Low plus High RH	419	82 (19.6)	1.28 (0.95,1.73)	0.099
13-29	Cholesterol-HDL Ratio	Comparison	1,154	375 (32.5)		
		Background RH	348	90 (25.9)	0.76 (0.58,0.99)	0.045
		Low RH	208	67 (32.2)	0.97 (0.71,1.34)	0.870
		High RH	211	84 (39.8)	1.32 (0.98,1.79)	0.070
		Low plus High RH	419	151 (36.0)	1.14 (0.90,1.44)	0.288
13-31	Triglycerides	Comparison	1,154	113 (9.8)		
		Background RH	348	28 (8.0)	0.85 (0.55,1.31)	0.461
		Low RH	208	32 (15.4)	1.65 (1.08,2.52)	0.021
		High RH	211	43 (20.4)	2.26 (1.53,3.34)	<0.001
		Low plus High RH	419	75 (17.9)	1.93 (1.40,2.66)	<0.001

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
13-33	Creatine Phosphokinase	Comparison	1,154	124	(10.7)		
		Background RH	348	32	(9.2)	0.94 (0.62,1.42)	0.772
		Low RH	208	18	(8.7)	0.75 (0.44,1.27)	0.282
		High RH	211	18	(8.5)	0.70 (0.41,1.18)	0.177
		Low plus High RH	419	36	(8.6)	0.72 (0.49,1.07)	0.107
13-35	Serum Amylase	Comparison	1,154	38	(3.3)		
		Background RH	348	8	(2.3)	0.61 (0.28,1.33)	0.217
		Low RH	208	8	(3.8)	1.21 (0.55,2.63)	0.638
		High RH	211	6	(2.8)	0.96 (0.40,2.30)	0.920
		Low plus High RH	419	14	(3.3)	1.07 (0.57,2.02)	0.827
13-36	Antibodies for Hepatitis A	Comparison	1,173	411	(35.0)		
		Background RH	350	104	(29.7)	0.79 (0.61,1.03)	0.077
		Low RH	210	70	(33.3)	0.92 (0.68,1.26)	0.622
		High RH	213	72	(33.8)	0.94 (0.69,1.28)	0.693
		Low plus High RH	423	142	(33.6)	0.93 (0.74,1.18)	0.559
13-37	Serological Evidence of Prior Hepatitis B Infection	Comparison	1,174	129	(11.0)		
		Background RH	352	15	(4.3)	0.38 (0.22,0.65)	<0.001
		Low RH	211	15	(7.1)	0.61 (0.35,1.06)	0.082
		High RH	213	20	(9.4)	0.81 (0.49,1.33)	0.394
		Low plus High RH	424	35	(8.3)	0.70 (0.47,1.04)	0.079
13-38	Antibodies for Hepatitis C	Comparison	1,174	19	(1.6)		
		Background RH	352	3	(0.9)	0.49 (0.14,1.68)	0.257
		Low RH	211	1	(0.5)	0.29 (0.04,2.21)	0.234
		High RH	213	1	(0.5)	0.30 (0.04,2.28)	0.246
		Low plus High RH	424	2	(0.5)	0.30 (0.07,1.29)	0.105
13-39	Stool Hemoccult	Comparison	1,078	15	(1.4)		
		Background RH	327	6	(1.8)	1.33 (0.51,3.48)	0.561
		Low RH	195	3	(1.5)	1.11 (0.32,3.86)	0.875
		High RH	199	3	(1.5)	1.08 (0.31,3.78)	0.904
		Low plus High RH	394	6	(1.5)	1.09 (0.42,2.85)	0.856
13-41	Prealbumin	Comparison	1,154	15	(1.3)		
		Background RH	348	8	(2.3)	1.67 (0.70,3.99)	0.251
		Low RH	208	5	(2.4)	1.90 (0.68,5.30)	0.218
		High RH	211	3	(1.4)	1.16 (0.33,4.07)	0.812
		Low plus High RH	419	8	(1.9)	1.49 (0.61,3.61)	0.382
13-43	Albumin	Comparison	1,154	6	(0.5)		
		Background RH	348	5	(1.4)	2.82 (0.84,9.46)	0.093
		Low RH	208	0	(0.0)	--	0.636[c]
		High RH	211	0	(0.0)	--	0.629[c]
		Low plus High RH	419	0	(0.0)	--	0.310[c]
13-45	α-1-Acid Glycoprotein	Comparison	1,154	55	(4.8)		
		Background RH	348	15	(4.3)	0.88 (0.49,1.59)	0.681
		Low RH	208	17	(8.2)	1.79 (1.02,3.15)	0.044
		High RH	211	13	(6.2)	1.33 (0.71,2.49)	0.368
		Low plus High RH	419	30	(7.2)	1.54 (0.97,2.45)	0.067

Table G-7. Summary of Unadjusted Results for Dichotomous Variables – Model 3
(Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
13-49	α-2-Macroglobulin	Comparison	1,154	163 (14.1)		
		Background RH	348	40 (11.5)	0.93 (0.64,1.36)	0.725
		Low RH	208	33 (15.9)	1.08 (0.71,1.65)	0.711
		High RH	211	31 (14.7)	0.90 (0.59,1.38)	0.631
		Low plus High RH	419	64 (15.3)	0.99 (0.71,1.36)	0.934
13-51	Apolipoprotein B	Comparison	1,154	26 (2.3)		
		Background RH	348	4 (1.1)	0.49 (0.17,1.41)	0.183
		Low RH	208	3 (1.4)	0.64 (0.19,2.14)	0.469
		High RH	211	2 (0.9)	0.43 (0.10,1.83)	0.252
		Low plus High RH	419	5 (1.2)	0.52 (0.20,1.40)	0.197
13-53	C3 Complement	Comparison	1,154	21 (1.8)		
		Background RH	348	8 (2.3)	1.10 (0.48,2.53)	0.818
		Low RH	208	0 (0.0)	--	0.098[c]
		High RH	211	1 (0.5)	0.29 (0.04,2.19)	0.231
		Low plus High RH	419	1 (0.2)	--	0.034[c]
13-55	C4 Complement	Comparison	1,154	91 (7.9)		
		Background RH	348	28 (8.0)	0.96 (0.61,1.49)	0.846
		Low RH	208	9 (4.3)	0.54 (0.27,1.08)	0.082
		High RH	211	20 (9.5)	1.30 (0.78,2.16)	0.319
		Low plus High RH	419	29 (6.9)	0.84 (0.53,1.32)	0.445
13-57	Haptoglobin	Comparison	1,154	134 (11.6)		
		Background RH	348	45 (12.9)	1.14 (0.79,1.63)	0.492
		Low RH	208	34 (16.3)	1.49 (0.99,2.24)	0.058
		High RH	211	27 (12.8)	1.11 (0.71,1.73)	0.639
		Low plus High RH	419	61 (14.6)	1.28 (0.92,1.78)	0.135
13-59	Transferrin	Comparison	1,154	72 (6.2)		
		Background RH	348	29 (8.3)	1.37 (0.87,2.15)	0.174
		Low RH	208	6 (2.9)	0.45 (0.19,1.04)	0.062
		High RH	211	7 (3.3)	0.51 (0.23,1.14)	0.100
		Low plus High RH	419	13 (3.1)	0.48 (0.26,0.88)	0.017
13-61	Prothrombin Time	Comparison	894	8 (0.9)		
		Background RH	269	1 (0.4)	0.51 (0.06,4.14)	0.529
		Low RH	145	3 (2.1)	1.69 (0.41,6.96)	0.465
		High RH	157	1 (0.6)	0.55 (0.07,4.50)	0.578
		Low plus High RH	302	4 (1.3)	0.94 (0.24,3.78)	0.935
14-3	Acne (Lifetime)	Comparison	1,174	477 (40.6)		
		Background RH	352	157 (44.6)	1.18 (0.92,1.50)	0.189
		Low RH	211	106 (50.2)	1.48 (1.10,1.98)	0.010
		High RH	213	105 (49.3)	1.42 (1.06,1.91)	0.019
		Low plus High RH	424	211 (49.8)	1.45 (1.16,1.81)	0.001
14-4	Post-SEA Acne	Comparison	1,173	239 (20.4)		
		Background RH	352	84 (23.9)	1.25 (0.94,1.66)	0.129
		Low RH	211	58 (27.5)	1.47 (1.06,2.06)	0.023
		High RH	213	62 (29.1)	1.58 (1.14,2.20)	0.006
		Low plus High RH	424	120 (28.3)	1.53 (1.18,1.97)	0.001

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
14-5	Post-SEA Acne (No Pre-SEA Acne)	Comparison	787	90 (11.4)		
		Background RH	227	32 (14.1)	1.28 (0.83,1.98)	0.272
		Low RH	132	27 (20.5)	1.99 (1.23,3.20)	0.005
		High RH	140	31 (22.1)	2.19 (1.39,3.46)	<0.001
		Low plus High RH	272	58 (21.3)	2.09 (1.45,3.01)	<0.001
14-6	Post-SEA Acne (with Pre-SEA Acne)	Comparison	386	149 (38.6)		
		Background RH	125	52 (41.6)	1.18 (0.78,1.78)	0.440
		Low RH	79	31 (39.2)	1.02 (0.62,1.67)	0.941
		High RH	73	31 (42.5)	1.15 (0.69,1.91)	0.600
		Low plus High RH	152	62 (40.8)	1.08 (0.73,1.58)	0.702
14-8	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (Excluding Participants with Pre-SEA Acne)	Comparison	89	26 (29.2)		
		Background RH	32	9 (28.1)	0.97 (0.39,2.40)	0.949
		Low RH	26	7 (26.9)	0.92 (0.34,2.48)	0.866
		High RH	30	10 (33.3)	1.20 (0.49,2.91)	0.693
		Low plus High RH	56	17 (30.4)	1.06 (0.51,2.20)	0.880
14-10	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (All Post-SEA Occurrences)	Comparison	236	82 (34.7)		
		Background RH	83	31 (37.3)	1.19 (0.70,2.02)	0.512
		Low RH	57	21 (36.8)	1.12 (0.61,2.04)	0.723
		High RH	61	21 (34.4)	0.94 (0.52,1.70)	0.833
		Low plus High RH	118	42 (35.6)	1.02 (0.64,1.62)	0.935
14-13	Acneiform Lesions	Comparison	1,174	58 (4.9)		
		Background RH	352	23 (6.5)	1.42 (0.86,2.35)	0.168
		Low RH	211	6 (2.8)	0.55 (0.23,1.30)	0.173
		High RH	213	16 (7.5)	1.49 (0.84,2.65)	0.177
		Low plus High RH	424	22 (5.2)	0.91 (0.52,1.57)	0.730
14-14	Acneiform Scars	Comparison	1,174	72 (6.1)		
		Background RH	352	27 (7.7)	1.32 (0.83,2.10)	0.241
		Low RH	211	11 (5.2)	0.83 (0.43,1.60)	0.580
		High RH	213	13 (6.1)	0.96 (0.52,1.78)	0.904
		Low plus High RH	424	24 (5.7)	0.90 (0.55,1.44)	0.650
14-15	Comedones	Comparison	1,174	79 (6.7)		
		Background RH	352	19 (5.4)	0.78 (0.46,1.31)	0.345
		Low RH	211	8 (3.8)	0.55 (0.26,1.15)	0.113
		High RH	213	13 (6.1)	0.91 (0.50,1.68)	0.769
		Low plus High RH	424	21 (5.0)	0.71 (0.43,1.18)	0.182
14-16	Depigmentation	Comparison	1,174	36 (3.1)		
		Background RH	352	4 (1.1)	0.39 (0.14,1.12)	0.080
		Low RH	211	7 (3.3)	1.05 (0.46,2.40)	0.906
		High RH	213	5 (2.3)	0.70 (0.27,1.83)	0.471
		Low plus High RH	424	12 (2.8)	0.86 (0.44,1.69)	0.661

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
14-17	Hyperpigmentation	Comparison	1,174	94 (8.0)		
		Background RH	352	18 (5.1)	0.72 (0.43,1.22)	0.221
		Low RH	211	18 (8.5)	1.00 (0.59,1.72)	0.992
		High RH	213	17 (8.0)	0.86 (0.50,1.49)	0.593
		Low plus High RH	424	35 (8.3)	0.93 (0.61,1.41)	0.727
14-18	Inclusion Cysts	Comparison	1,174	134 (11.4)		
		Background RH	352	43 (12.2)	1.10 (0.76,1.59)	0.614
		Low RH	211	23 (10.9)	0.94 (0.59,1.51)	0.811
		High RH	213	31 (14.6)	1.30 (0.85,1.99)	0.222
		Low plus High RH	424	54 (12.7)	1.11 (0.79,1.56)	0.550
14-19	Dermatology Index	Comparison	1,174	277 (23.6)		
		Background RH	352	84 (23.9)	1.05 (0.79,1.39)	0.742
		Low RH	211	40 (19.0)	0.75 (0.52,1.09)	0.127
		High RH	213	59 (27.7)	1.21 (0.87,1.68)	0.266
		Low plus High RH	424	99 (23.3)	0.95 (0.73,1.24)	0.717
15-3	Essential Hypertension	Comparison	1,146	644 (56.2)		
		Background RH	345	168 (48.7)	0.89 (0.69,1.14)	0.356
		Low RH	202	109 (54.0)	0.87 (0.63,1.19)	0.380
		High RH	211	135 (64.0)	1.19 (0.87,1.64)	0.282
		Low plus High RH	413	244 (59.1)	1.02 (0.80,1.30)	0.869
15-4	Heart Disease (Excluding Essential Hypertension)	Comparison	1.156	937 (81.1)		
		Background RH	348	299 (85.9)	1.50 (1.07,2.11)	0.019
		Low RH	206	171 (83.0)	1.13 (0.76,1.67)	0.544
		High RH	212	173 (81.6)	0.99 (0.68,1.45)	0.963
		Low plus High RH	418	344 (82.3)	1.06 (0.79,1.42)	0.710
15-5	Myocardial Infarction	Comparison	1,156	132 (11.4)		
		Background RH	348	34 (9.8)	0.86 (0.58,1.29)	0.469
		Low RH	206	18 (8.7)	0.74 (0.44,1.24)	0.249
		High RH	212	24 (11.3)	0.97 (0.61,1.54)	0.885
		Low plus High RH	418	42 (10.0)	0.85 (0.58,1.22)	0.376
15-6	Stroke or Transient Ischemic Attack	Comparison	1,156	36 (3.1)		
		Background RH	348	12 (3.4)	1.16 (0.59,2.27)	0.660
		Low RH	206	7 (3.4)	1.08 (0.47,2.47)	0.851
		High RH	212	10 (4.7)	1.48 (0.72,3.04)	0.287
		Low plus High RH	418	17 (4.1)	1.27 (0.70,2.30)	0.435
15-8	Systolic Blood Pressure	Comparison	1,156	301 (26.0)		
		Background RH	347	90 (25.9)	1.06 (0.80,1.40)	0.674
		Low RH	206	40 (19.4)	0.67 (0.46,0.97)	0.035
		High RH	212	45 (21.2)	0.72 (0.50,1.03)	0.072
		Low plus High RH	418	85 (20.3)	0.70 (0.53,0.92)	0.010

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
15-10	Diastolic Blood Pressure	Comparison	1,156	56 (4.8)		
		Background RH	347	13 (3.7)	0.77 (0.41,1.43)	0.409
		Low RH	206	9 (4.4)	0.90 (0.44,1.84)	0.764
		High RH	212	19 (9.0)	1.92 (1.11,3.31)	0.019
		Low plus High RH	418	28 (6.7)	1.32 (0.81,2.15)	0.267
15-11	Heart Sounds	Comparison	1,156	69 (6.0)		
		Background RH	347	23 (6.6)	1.19 (0.73,1.95)	0.481
		Low RH	206	14 (6.8)	1.13 (0.62,2.05)	0.687
		High RH	212	15 (7.1)	1.13 (0.63,2.03)	0.678
		Low plus High RH	418	29 (6.9)	1.13 (0.72,1.78)	0.593
15-12	Overall ECG	Comparison	1,156	409 (35.4)		
		Background RH	347	134 (38.6)	1.24 (0.96,1.59)	0.096
		Low RH	206	75 (36.4)	1.03 (0.75,1.40)	0.861
		High RH	212	66 (31.1)	0.77 (0.56,1.06)	0.110
		Low plus High RH	418	141 (33.7)	0.89 (0.70,1.13)	0.333
15-13	ECG: RBBB	Comparison	1,156	42 (3.6)		
		Background RH	347	19 (5.5)	1.52 (0.87,2.66)	0.142
		Low RH	206	5 (2.4)	0.66 (0.26,1.69)	0.388
		High RH	212	8 (3.8)	1.05 (0.48,2.27)	0.903
		Low plus High RH	418	13 (3.1)	0.84 (0.44,1.59)	0.586
15-14	ECG: LBBB	Comparison	1,156	16 (1.4)		
		Background RH	347	5 (1.4)	1.21 (0.44,3.37)	0.713
		Low RH	206	1 (0.5)	0.33 (0.04,2.52)	0.286
		High RH	212	2 (0.9)	0.58 (0.13,2.58)	0.477
		Low plus High RH	418	3 (0.7)	0.44 (0.12,1.62)	0.218
15-15	ECG: Nonspecific ST- and T-wave Changes	Comparison	1,156	269 (23.3)		
		Background RH	347	82 (23.6)	1.12 (0.84,1.50)	0.426
		Low RH	206	44 (21.4)	0.87 (0.61,1.25)	0.462
		High RH	212	53 (25.0)	1.01 (0.72,1.43)	0.951
		Low plus High RH	418	97 (23.2)	0.94 (0.72,1.23)	0.652
15-16	ECG: Bradycardia	Comparison	1,156	51 (4.4)		
		Background RH	347	27 (7.8)	1.69 (1.04,2.76)	0.034
		Low RH	206	11 (5.3)	1.24 (0.64,2.43)	0.524
		High RH	212	6 (2.8)	0.68 (0.29,1.60)	0.374
		Low plus High RH	418	17 (4.1)	0.91 (0.51,1.64)	0.760
15-17	ECG: Tachycardia	Comparison	1,156	7 (0.6)		
		Background RH	347	2 (0.6)	0.92 (0.19,4.51)	0.920
		Low RH	206	0 (0.0)	--	0.555[c]
		High RH	212	1 (0.5)	0.80 (0.10,6.59)	0.836
		Low plus High RH	418	1 (0.2)	--	0.616[c]
15-18	ECG: Arrhythmia	Comparison	1,156	125 (10.8)		
		Background RH	347	34 (9.8)	0.98 (0.66,1.47)	0.941
		Low RH	206	25 (12.1)	1.11 (0.70,1.76)	0.649
		High RH	212	13 (6.1)	0.49 (0.27,0.89)	0.019
		Low plus High RH	418	38 (9.1)	0.73 (0.49,1.10)	0.131

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
15-19	ECG: Evidence of Prior Myocardial Infarction	Comparison	1,156	61	(5.3)		
		Background RH	347	16	(4.6)	0.90 (0.51,1.60)	0.730
		Low RH	206	10	(4.9)	0.91 (0.46,1.80)	0.778
		High RH	212	8	(3.8)	0.68 (0.32,1.44)	0.312
		Low plus High RH	418	18	(4.3)	0.78 (0.45,1.35)	0.374
15-20	Funduscopic Examination	Comparison	1,063	107	(10.1)		
		Background RH	320	34	(10.6)	1.17 (0.78,1.77)	0.448
		Low RH	182	22	(12.1)	1.21 (0.74,1.98)	0.450
		High RH	195	24	(12.3)	1.15 (0.71,1.86)	0.562
		Low plus High RH	377	46	(12.2)	1.18 (0.81,1.71)	0.384
15-21	Carotid Bruits	Comparison	1,156	29	(2.5)		
		Background RH	347	9	(2.6)	1.07 (0.50,2.29)	0.865
		Low RH	206	2	(1.0)	0.38 (0.09,1.60)	0.186
		High RH	212	3	(1.4)	0.54 (0.16,1.80)	0.318
		Low plus High RH	418	5	(1.2)	0.45 (0.17,1.20)	0.111
15-22	Radial Pulses	Comparison	1,148	82	(7.1)		
		Background RH	347	27	(7.8)	1.12 (0.71,1.77)	0.619
		Low RH	205	8	(3.9)	0.52 (0.25,1.10)	0.089
		High RH	212	13	(6.1)	0.83 (0.45,1.53)	0.552
		Low plus High RH	417	21	(5.0)	0.66 (0.40,1.10)	0.110
15-23	Femoral Pulses	Comparison	1,156	9	(0.8)		
		Background RH	348	4	(1.1)	1.51 (0.46,4.98)	0.496
		Low RH	206	5	(2.4)	3.15 (1.05,9.51)	0.041
		High RH	212	3	(1.4)	1.79 (0.48,6.72)	0.385
		Low plus High RH	418	8	(1.9)	2.37 (0.89,6.32)	0.085
15-24	Popliteal Pulses	Comparison	1,155	30	(2.6)		
		Background RH	348	6	(1.7)	0.68 (0.28,1.66)	0.398
		Low RH	205	6	(2.9)	1.12 (0.46,2.73)	0.802
		High RH	211	5	(2.4)	0.88 (0.34,2.31)	0.798
		Low plus High RH	416	11	(2.6)	0.99 (0.49,2.01)	0.983
15-25	Dorsalis Pedis Pulses	Comparison	1,152	96	(8.3)		
		Background RH	347	25	(7.2)	0.89 (0.56,1.41)	0.623
		Low RH	205	16	(7.8)	0.92 (0.53,1.60)	0.771
		High RH	212	19	(9.0)	1.04 (0.62,1.75)	0.877
		Low plus High RH	417	35	(8.4)	0.98 (0.65,1.47)	0.926
15-26	Posterior Tibial Pulses	Comparison	1,153	68	(5.9)		
		Background RH	348	14	(4.0)	0.66 (0,37,1.20)	0.173
		Low RH	205	7	(3.4)	0.57 (0.26,1.25)	0.158
		High RH	211	11	(5.2)	0.88 (0.46,1.71)	0.714
		Low plus High RH	416	18	(4.3)	0.71 (0.41,1.22)	0.215
15-27	Leg Pulses	Comparison	1,152	114	(9.9)		
		Background RH	347	27	(7.8)	0.79 (0.51,1.23)	0.299
		Low RH	204	17	(8.3)	0.82 (0.48,1.40)	0.470
		High RH	211	21	(10.0)	0.98 (060,1.60)	0.935
		Low plus High RH	415	38	(9.2)	0.90 (0.61,1.32)	0.588

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
15-28	Peripheral Pulses	Comparison	1,145	182 (15.9)		
		Background RH	346	49 (14.2)	0.90 (0.64,1.27)	0.551
		Low RH	203	22 (10.8)	0.64 (0.40,1.02)	0.061
		High RH	211	34 (16.1)	0.99 (0.66,1.48)	0.958
		Low plus High RH	414	56 (13.5)	0.80 (0.57,1.11)	0.178
15-30	Resting Pressure Index	Comparison	1,138	40 (3.5)		
		Background RH	347	13 (3.7)	1.09 (0.57,2.06)	0.801
		Low RH	206	8 (3.9)	1.10 (0.51,2.39)	0.802
		High RH	209	11 (5.3)	1.50 (0.75,2.99)	0.247
		Low plus High RH	415	19 (4.6)	1.29 (0.73,2.27)	0.378
15-32	Hyperemic Pressure Index (1 Minute Post-exercise)	Comparison	1,108	103 (9.3)		
		Background RH	340	31 (9.1)	1.02 (0.67,1.56)	0.925
		Low RH	199	20 (10.1)	1.08 (0.65,1.79)	0.760
		High RH	200	21 (10.5)	1.10 (0.67,1.81)	0.711
		Low plus High RH	399	41 (10.3)	1.09 (0.74,1.60)	0.658
15-34	Hyperemic Pressure Index (2 Minutes Post-exercise)	Comparison	1,110	65 (5.9)		
		Background RH	340	17 (5.0)	0.84 (0.49,1.47)	0.549
		Low RH	199	8 (4.0)	0.67 (0.32,1.43)	0.302
		High RH	200	9 (4.5)	0.76 (0.37,1.55)	0.450
		Low plus High RH	399	17 (4.3)	0.71 (0.41,1.24)	0.230
15-35	Intermittent Claudication and Vascular Insufficiency Index	Comparison	1,154	37 (3.2)		
		Background RH	348	10 (2.9)	0.98 (0.48,2.00)	0.949
		Low RH	206	4 (1.9)	0.58 (0.21,1.65)	0.310
		High RH	212	8 (3.8)	1.09 (0.50,2.38)	0.833
		Low plus High RH	418	12 (2.9)	0.80 (0.40,1.60)	0.526
16-13	RBC Morphology	Comparison	1,171	61 (5.2)		
		Background RH	351	19 (5.4)	1.05 (0.62,1.80)	0.846
		Low RH	210	18 (8.6)	1.70 (0.98,2.94)	0.058
		High RH	209	14 (6.7)	1.29 (0.71,2.36)	0.405
		Low plus High RH	419	32 (7.6)	1.48 (0.95,2.32)	0.084
16-16	Absolute Neutrophils (Bands) (Zero vs. Nonzero)	Comparison	1,171	239 (20.4)		
		Background RH	351	60 (17.1)	0.79 (0.58,1.09)	0.150
		Low RH	210	47 (22.4)	1.13 (0.79,1.61)	0.505
		High RH	209	38 (18.2)	0.88 (0.60,1.28)	0.496
		Low plus High RH	419	85 (20.3)	0.99 (0.75,1.31)	0.969
16-20	Absolute Eosinophils (Zero vs. Nonzero)	Comparison	1,171	126 (10.8)		
		Background RH	351	31 (8.8)	0.82 (0.54,1.24)	0.341
		Low RH	210	25 (11.9)	1.12 (0.71,1.76)	0.639
		High RH	209	16 (7.7)	0.68 (0.39,1.17)	0.160
		Low plus High RH	419	41 (9.8)	0.87 (0.60,1.27)	0.470
16-22	Absolute Basophils (Zero vs. Nonzero)	Comparison	1,171	551 (47.1)		
		Background RH	351	170 (48.4)	1.04 ((0.81,1.32)	0.773
		Low RH	210	102 (48.6)	1.07 (0.80,1.43)	0.660
		High RH	209	101 (48.3)	1.07 (0.80,1.44)	0.648
		Low plus High RH	419	203 (48.4)	1.07 (0.86,1.34)	0.555

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
16-24	Fibrinogen	Comparison	1,171	62 (5.3)		
		Background RH	350	21 (6.0)	1.25 (0.75,2.09)	0.395
		Low RH	210	16 (7.6)	1.43 (0.81,2.54)	0.219
		High RH	209	12 (5.7)	1.00 (0.53,1.91)	0.991
		Low plus High RH	419	28 (6.7)	1.20 (0.75,1.91)	0.445
16-26	Erythrocyte Sedimentation Rate	Comparison	1,171	117 (10.0)		
		Background RH	351	36 (10.3)	1.17 (0.78,1.74)	0.444
		Low RH	210	28 (13.3)	1.33 (0.85,2.09)	0.206
		High RH	209	26 (12.4)	1.15 (0.72,1.82)	0.560
		Low plus High RH	419	54 (12.9)	1.24 (0.87,1.75)	0.232
17-3	Occurrence of Kidney Stones	Comparison	1,162	119 (10.2)		
		Background RH	348	36 (10.3)	1.03 (0.69,1.54)	0.873
		Low RH	208	32 (15.4)	1.58 (1.04,2.42)	0.033
		High RH	211	18 (8.5)	0.80 (0.48,1.35)	0.408
		Low plus High RH	419	50 (11.9)	1.12 (0.78,1.61)	0.525
17-4	Occurrence of Past Kidney Disease	Comparison	1,153	436 (37.8)		
		Background RH	346	121 (35.0)	0.96 (0.74,1.24)	0.740
		Low RH	208	75 (36.1)	0.90 (0.66,1.23)	0.523
		High RH	209	75 (35.9)	0.86 (0.63,1.18)	0.350
		Low plus High RH	417	150 (36.0)	0.88 (0.70,1.12)	0.299
17-9	Urinary Micro-albumin to Urinary Creatinine Ratio (Nonzero vs. Zero)	Comparison	1,174	141 (12.0)		
		Background RH	352	42 (11.9)	1.09 (0.75,1.58)	0.645
		Low RH	211	35 (16.6)	1.42 (0.94,2.13)	0.093
		High RH	213	29 (13.6)	1.06 (0.69,1.64)	0.782
		Low plus High RH	424	64 (15.1)	1.23 (0.89,1.69)	0.216
17-11	Urinary Occult Blood	Comparison	1,174	25 (2.1)		
		Background RH	352	9 (2.6)	1.26 (0.58,2.75)	0.555
		Low RH	211	9 (4.3)	2.02 (0.93,4.39)	0.077
		High RH	213	4 (1.9)	0.84 (0.29,2.46)	0.755
		Low plus High RH	424	13 (3.1)	1.30 (0.63,2.67)	0.473
17-12	Urinary WBC Count	Comparison	1,174	65 (5.5)		
		Background RH	352	21 (6.0)	1.12 (0.67,1.86)	0.667
		Low RH	211	18 (8.5)	1.58 (0.91,2.72)	0.102
		High RH	213	16 (7.5)	1.35 (0.76,2.38)	0.306
		Low plus High RH	424	34 (8.0)	1.46 (0.94,2.24)	0.089
17-13	Urinary Protein	Comparison	1,174	49 (4.2)		
		Background RH	352	11 (3.1)	0.90 (0.46,1.76)	0.754
		Low RH	211	7 (3.3)	0.70 (0.31,1.60)	0.401
		High RH	213	8 (3.8)	0.74 (0.34,1.61)	0.443
		Low plus High RH	424	15 (3.5)	0.72 (0.39,1.32)	0.287
18-3	Past Thyroid Disease	Comparison	1,167	152 (13.0)		
		Background RH	349	42 (12.0)	0.94 (0.65,1.36)	0.754
		Low RH	209	21 (10.0)	0.74 (0.46,1.20)	0.220
		High RH	211	20 (9.5)	0.68 (0.41,1.11)	0.124
		Low plus High RH	420	41 (9.8)	0.71 (0.49,1.02)	0.065

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
18-4	Composite Diabetes Indicator (2002 AFHS Diabetes Definition)	Comparison	1,173	226 (19.3)		
		Background RH	352	42 (11.9)	0.71 (0.49,1.03)	0.073
		Low RH	210	47 (22.4)	1.14 (0.78,1.68)	0.496
		High RH	213	52 (24.4)	1.13 (0.78,1.63)	0.531
		Low plus High RH	423	99 (23.4)	1.13 (0.85,1.51)	0.392
18-5	Composite Diabetes Indicator (Pre-2002 AFHS Diabetes Definition)	Comparison	1,173	259 (22.1)		
		Background RH	352	52 (14.8)	0.76 (0.54,1.08)	0.123
		Low RH	210	50 (23.8)	1.04 (0.71,1.50)	0.855
		High RH	213	58 (27.2)	1.10 (0.77,1.58)	0.584
		Low plus High RH	423	108 (25.5)	1.07 (0.81,1.41)	0.635
18-8	Time to Diabetes Onset (years) (2002 AFHS Diabetes Definition)	Comparison	1,173	28.41[d]		
		Background RH	352	33.17[d]	0.67 (0.48,0.93)[e]	0.017[e]
		Low RH	210	25.75[d]	1.14 (0.84,1.57)[e]	0.401[e]
		High RH	213	23.67[d]	1.07 (0.79,1.45)[e]	0.661[e]
		Low plus High RH	423	25.08[d]	1.10 (0.87,1.40)[e]	0.413[e]
18-9	Time to Diabetes Onset (years) (Pre-2002 AFHS Diabetes Definition)	Comparison	1,173	28.41[d]		
		Background RH	352	33.08[d]	0.69 (0.51,0.93)[e]	0.016[e]
		Low RH	210	25.75[d]	1.09 (0.80,1.47)[e]	0.593[e]
		High RH	213	23.67[d]	1.03 (0.77,1.37)[e]	0.858[e]
		Low plus High RH	423	25.08[d]	1.05 (0.84,1.32)[e]	0.651[e]
18-10	Thyroid Gland	Comparison	1,093	24 (2.2)		
		Background RH	329	6 (1.8)	0.81 (0.33,2.01)	0.649
		Low RH	201	2 (1.0)	0.45 (0.11,1.92)	0.281
		High RH	203	0 (0.0)	--	0.065[c]
		Low plus High RH	404	2 (0.5)	--	0.044[c]
18-11	Testicular Examination	Comparison	1,158	78 (6.7)		
		Background RH	347	24 (6.9)	1.04 (0.65,1.68)	0.862
		Low RH	206	14 (6.8)	1.01 (0.56,1.81)	0.985
		High RH	210	18 (8.6)	1.28 (0.75,2.20)	0.361
		Low plus High RH	416	32 (7.7)	1.14 (0.74,1.75)	0.557
18-15	Free T_4	Comparison	1,089	113 (10.4)		
		Background RH	328	30 (9.1)	0.91 (0.59,1.39)	0.666
		Low RH	201	20 (10.0)	0.94 (0.57,1.55)	0.804
		High RH	203	17 (8.4)	0.75 (0.44,1.29)	0.297
		Low plus High RH	404	37 (9.2)	0.84 (0.57,1.24)	0.383
18-16	Anti-thyroid Antibodies	Comparison	1,089	6 (0.6)		
		Background RH	328	1 (0.3)	0.56 (0.07,4.74)	0.508
		Low RH	201	2 (1.0)	1.80 (0.36,9.00)	0.474
		High RH	203	1 (0.5)	0.87 (0.10,7.36)	0.901
		Low plus High RH	404	3 (0.7)	1.25 (0.29,5.36)	0.762
18-18	Fasting Glucose	Comparison	1,173	236 (20.1)		
		Background RH	352	62 (17.6)	1.05 (0.76,1.45)	0.775
		Low RH	210	53 (25.2)	1.29 (0.90,1.85)	0.166
		High RH	213	49 (23.0)	1.00 (0.69,1.45)	0.990
		Low plus High RH	423	102 (24.1)	1.14 (0.86,1.50)	0.369

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
18-20	2-hour Postprandial Glucose (Nondiabetics Only)	Comparison	936	198 (21.2)		
		Background RH	308	62 (20.1)	1.00 (0.73,1.39)	0.980
		Low RH	161	40 (24.8)	1.25 (0.84,1.85)	0.269
		High RH	159	31 (19.5)	0.84 (0.55,1.28)	0.418
		Low plus High RH	320	71 (22.2)	1.02 (0.75,1.40)	0.879
18-21	2-hour Postprandial Urinary Glucose (Nondiabetics Only)	Comparison	936	242 (25.9)		
		Background RH	308	88 (28.6)	1.14 (0.85,1.52)	0.370
		Low RH	161	39 (24.2)	0.92 (0.62,1.35)	0.659
		High RH	159	44 (27.7)	1.10 (0.76,1.61)	0.609
		Low plus High RH	320	83 (25.9)	1.01 (0.75,1.34)	0.973
18-27	Hemoglobin A1c (Diabetics Only)	Comparison	221	146 (66.1)		
		Background RH	42	22 (52.4)	0.59 (0.30,1.16)	0.129
		Low RH	46	30 (65.2)	0.92 (0.47,1.80)	0.808
		High RH	51	38 (74.5)	1.48 (0.74,2.96)	0.264
		Low plus High RH	97	68 (70.1)	1.18 (0.70,1.99)	0.530
18-29	C-peptide (Diabetics Only)	Comparison	221	56 (25.3)		
		Background RH	42	8 (19.0)	0.82 (0.35,1.90)	0.643
		Low RH	46	17 (37.0)	1.49 (0.75,2.99)	0.256
		High RH	51	11 (21.6)	0.73 (0.34,1.56)	0.416
		Low plus High RH	97	28 (28.9)	1.03 (0.58,1.80)	0.931
18-31	Proinsulin (Diabetics Only)	Comparison	221	104 (47.1)		
		Background RH	42	17 (40.5)	0.94 (0.47,1.89)	0.873
		Low RH	46	27 (58.7)	1.37 (0.70,2.69)	0.353
		High RH	51	29 (56.9)	1.45 (0.76,2.76)	0.257
		Low plus High RH	97	56 (57.7)	1.41 (0.86,2.34)	0.176
18-32	GADA (Diabetics Only)	Comparison	221	9 (4.1)		
		Background RH	42	0 (0.0)	--	0.386[c]
		Low RH	46	2 (4.3)	1.15 (0.24,5.58)	0.859
		High RH	51	1 (2.0)	0.48 (0.06,3.86)	0.488
		Low plus High RH	97	3 (3.1)	0.73 (0.18,2.97)	0.655
18-34	Total Testosterone	Comparison	1,161	165 (14.2)		
		Background RH	349	52 (14.9)	1.25 (0.89,1.77)	0.200
		Low RH	210	35 (16.7)	1.14 (0.76,1.72)	0.527
		High RH	210	41 (19.5)	1.29 (0.87,1.90)	0.207
		Low plus High RH	420	76 (18.1)	1.21 (0.89,1.65)	0.221
18-36	Free Testosterone	Comparison	1,161	64 (5.5)		
		Background RH	349	22 (6.3)	1.41 (0.85,2.36)	0.184
		Low RH	210	14 (6.7)	1.11 (0.60,2.06)	0.733
		High RH	210	13 (6.2)	0.94 (0.50,1.76)	0.836
		Low plus High RH	420	27 (6.4)	1.02 (0.63,1.65)	0.934

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
18-38	Estradiol	Comparison	1,161	30 (2.6)		
		Background RH	349	14 (4.0)	1.67 (0.87,3.21)	0.123
		Low RH	210	3 (1.4)	0.53 (0.16,1.77)	0.305
		High RH	210	6 (2.9)	1.05 (0.43,2.57)	0.912
		Low plus High RH	420	9 (2.1)	0.75 (0.34,1.65)	0.475
18-40	LH	Comparison	1,161	69 (5.9)		
		Background RH	349	18 (5.2)	0.89 (0.52,1.53)	0.677
		Low RH	210	9 (4.3)	0.70 (0.34,1.43)	0.325
		High RH	210	8 (3.8)	0.61 (0.29,1.28)	0.191
		Low plus High RH	420	17 (4.0)	0.65 (0.38,1.12)	0.124
18-42	FSH	Comparison	1,161	70 (6.0)		
		Background RH	349	22 (6.3)	1.08 (0.66,1.78)	0.758
		Low RH	210	15 (7.1)	1.19 (0.67,2.12)	0.562
		High RH	210	7 (3.3)	0.52 (0.24,1.16)	0.109
		Low plus High RH	420	22 (5.2)	0.79 (0.47,1.33)	0.368
19-14	Lupus Panel: ANA Test	Comparison	1,068	204 (19.1)		
		Background RH	317	59 (18.6)	0.96 (0.70,1.33)	0.829
		Low RH	187	31 (16.6)	0.84 (0.56,1.27)	0.416
		High RH	190	43 (22.6)	1.24 (0.85,1.81)	0.255
		Low plus High RH	377	74 (19.6)	1.02 (0.76,1.38)	0.875
19-15	Lupus Panel: Thyroid Microsomal Antibody	Comparison	1,068	24 (2.2)		
		Background RH	317	10 (3.2)	1.46 (0.69,3.11)	0.327
		Low RH	187	6 (3.2)	1.44 (0.58,3.57)	0.434
		High RH	190	7 (3.7)	1.63 (0.69,3.85)	0.267
		Low plus High RH	377	13 (3.4)	1.53 (0.77,3.04)	0.226
19-16	Lupus Panel: MSK Antismooth Muscle Antibody	Comparison	1,068	8 (0.7)		
		Background RH	317	6 (1.9)	3.22 (1.08,9.55)	0.035
		Low RH	187	3 (1.6)	2.04 (0.53,7.88)	0.300
		High RH	190	0 (0.0)	--	0.483[c]
		Low plus High RH	377	3 (0.8)	--	0.999[c]
19-17	Lupus Panel: MSK Antiparietal Cell Antibody	Comparison	1,068	2 (0.2)		
		Background RH	317	1 (0.3)	1.67 (0.15,18.95)	0.679
		Low RH	187	1 (0.5)	2.87 (0.26,31.81)	0.391
		High RH	190	0 (0.0)	--	0.999[c]
		Low plus High RH	377	1 (0.3)	--	0.999[c]
19-18	Lupus Panel: MSK Antiparietal Cell Antibody	Comparison	1,068	33 (3.1)		
		Background RH	317	9 (2.8)	1.07 (0.50,2.28)	0.867
		Low RH	187	4 (2.1)	0.66 (0.23,1.91)	0.446
		High RH	190	3 (1.6)	0.44 (0.13,1.48)	0.186
		Low plus High RH	377	7 (1.9)	0.54 (0.23,1.25)	0.152
19-19	Lupus Panel: Rheumatoid Factor	Comparison	1,068	216 (20.2)		
		Background RH	317	73 (23.0)	1.20 (0.89,1.63)	0.233
		Low RH	187	60 (32.1)	1.86 (1.32,2.62)	<0.001
		High RH	190	33 (17.4)	0.82 (0.54,1.23)	0.328
		Low plus High RH	377	93 (24.7)	1.23 (0.92,1.64)	0.158

Table Ref.	Clinical Parameter	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
20-3	Asthma	Comparison	1,168	75 (6.4)		
		Background RH	349	27 (7.7)	1.25 (0.79,1.99)	0.335
		Low RH	207	12 (5.8)	0.89 (0.47,1.67)	0.715
		High RH	211	11 (5.2)	0.78 (0.41,1.50)	0.462
		Low plus High RH	418	23 (5.5)	0.83 (0.51,1.35)	0.461
20-4	Bronchitis	Comparison	1,151	352 (30.6)		
		Background RH	343	108 (31.5)	1.07 (0.82,1.39)	0.629
		Low RH	203	67 (33.0)	1.11 (0.81,1.53)	0.513
		High RH	209	66 (31.6)	1.03 (0.75,1.41)	0.870
		Low plus High RH	412	133 (32.3)	1.07 (0.84,1.36)	0.594
20-5	Pneumonia	Comparison	1,133	161 (14.2)		
		Background RH	333	43 (12.9)	0.92 (0.64,1.32)	0.654
		Low RH	195	31 (15.9)	1.13 (0.74,1.72)	0.569
		High RH	208	23 (11.1)	0.73 (0.46,1.17)	0.189
		Low plus High RH	403	54 (13.4)	0.90 (0.64,1.26)	0.551
20-6	Thorax and Lung Abnormality	Comparison	1,174	197 (16.8)		
		Background RH	351	67 (19.1)	1.14 (0.84,1.56)	0.401
		Low RH	211	45 (21.3)	1.35 (0.94,1.95)	0.103
		High RH	213	46 (21.6)	1.40 (0.97,2.01)	0.071
		Low plus High RH	424	91 (21.5)	1.37 (1.04,1.82)	0.025
20-7	X-ray Interpretation	Comparison	1,174	205 (17.5)		
		Background RH	350	53 (15.1)	0.84 (0.61,1.17)	0.312
		Low RH	211	38 (18.0)	1.04 (0.71,1.52)	0.847
		High RH	212	27 (12.7)	0.69 (0.45,1.06)	0.093
		Low plus High RH	423	65 (15.4)	0.85 (0.62,1.15)	0.288
20-9	FVC	Comparison	1,161	116 (10.0)		
		Background RH	348	27 (7.8)	0.87 (0.56,1.36)	0.545
		Low RH	207	27 (13.0)	1.30 (0.83,2.05)	0.255
		High RH	212	17 (8.0)	0.68 (0.40,1.17)	0.168
		Low plus High RH	419	44 (10.5)	0.94 (0.64,1.37)	0.749
20-11	FEV$_1$	Comparison	1,161	341 (29.4)		
		Background RH	348	103 (29.6)	1.04 (0.80,1.36)	0.769
		Low RH	207	76 (36.7)	1.39 (1.02,1.89)	0.039
		High RH	212	61 (28.8)	0.95 (0.68,1.31)	0.742
		Low plus High RH	419	137 (32.7)	1.14 (0.90,1.46)	0.278

[a]Adjusted for body mass index at the time of the blood measurement for dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormalities.
[d]10th percentile based on proportional hazards model was given for time to diabetes onset variable.
[e]Hazard ratio, confidence interval, and p-value, based on proportional hazards model, were given for time to diabetes onset variable.

--: Relative risk, confidence interval, and p-value were not presented because of the sparse number of participants
with abnormalities.

Note: RH = Ranch Hand.
Background: (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table G-8. Summary of Unadjusted Results for Dichotomous Variables – Model 4 (Ranch Hands: Log$_2$ (1987 Dioxin))

Table Ref.	Clinical Parameter	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
9-3	Self-perception of Health	1.13 (1.00,1.28)	0.055
9-4	Appearance of Illness or Distress	0.99 (0.79,1.24)	0.928
9-5	Relative Age Appearance	1.34 (1.11,1.62)	0.002
9-7	Body Mass Index	1.31 (1.19,1.44)	<0.001
10-3	All Skin Neoplasms	0.97 (0.89,1.07)	0.559
10-4	Malignant Skin Neoplasms	0.94 (0.85,1.05)	0.261
10-5	Benign Skin Neoplasms	0.98 (0.90,1.07)	0.686
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	0.87 (0.56,1.35)	0.531
10-7	Basal Cell Carcinoma	0.89 (0.80,1.00)	0.051
10-8	Squamous Cell Carcinoma	0.99 (0.82,1.20)	0.928
10-9	Nonmelanoma	0.92 (0.83,1.02)	0.118
10-10	Melanoma	1.07 (0.82,1.42)	0.611
10-11	Systemic Neoplasms	0.98 (0.89,1.08)	0.689
10-12	Malignant Systemic Neoplasms	0.91 (0.79,1.04)	0.166
10-13	Benign Systemic Neoplasms	1.00 (0.91,1.11)	0.951
10-14	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	0.94 (0.68,1.30)	0.722
10-16	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	2.35 (0.72,7.62)	0.144
10-17	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	1.04 (0.57,1.91)	0.889
10-18	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	0.40 (0.17,0.92)	0.038
10-19	Malignant Systemic Neoplasms (Thyroid Gland)	0.93 (0.27,3.22)	0.912
10-20	Malignant Systemic Neoplasms (Bronchus and Lung)	1.10 (0.79,1.54)	0.567
10-21	All Stomach Neoplasms	1.14 (0.70,1.85)	0.600
10-22	Malignant Systemic Neoplasms (Colon and Rectum)	1.11 (0.78,1.57)	0.559
10-23	Malignant Systemic Neoplasms (Urinary System)	0.89 (0.66,1.20)	0.438
10-24	Malignant Systemic Neoplasms (Kidney and Ureter)	0.69 (0.43,1.13)	0.138
10-25	Malignant Systemic Neoplasms (Prostate)	0.88 (0.74,1.05)	0.157
10-26	Malignant Systemic Neoplasms (Penis and Other Male Genital Organs)	2.22 (0.97,5.09)	0.053
10-27	Malignant Systemic Neoplasms (Testicles)	1.23 (0.63,2.41)	0.551
10-28	Malignant Systemic Neoplasms (Bone and Articular Cartilage)	--	--
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	2.35 (0.72,7.62)	0.144
10-30	Carcinoma in Situ	1.03 (0.56,1.88)	0.933
10-31	Hodgkin's Disease	0.73 (0.20,2.62)	0.628
10-32	Leukemia	0.43 (0.23,0.79)	0.008
10-33	Other Malignant Systemic Neoplasms (Lymphoid and Histiocytic Tissue)	0.91 (0.55,1.52)	0.727
10-34	Lymphoreticular Sarcoma	0.83 (0.24,2.95)	0.776
10-35	Skin and Systemic Neoplasms	0.96 (0.87,1.05)	0.385
10-36	Malignant Skin and Systemic Neoplasms	0.92 (0.84,1.01)	0.091
10-38	PSA	0.84 (0.67,1.05)	0.115
11-3	Inflammatory Diseases	0.93 (0.61,1.41)	0.727
11-4	Hereditary and Degenerative Diseases	0.98 (0.87,1.10)	0.752
11-5	Peripheral Disorders	1.09 (0.99,1.21)	0.072
11-6	Other Neurological Disorders	1.16 (1.04,1.30)	0.007
11-7	Smell	0.71 (0.53,0.95)	0.018
11-8	Visual Fields	0.75 (0.52,1.09)	0.126
11-9	Light Reaction	1.01 (0.55,1.87)	0.971

Table Ref.	Clinical Parameter	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
11-10	Ocular Movement	0.91 (0.52,1.60)	0.746
11-11	Facial Sensation	0.99 (0.53,1.83)	0.967
11-12	Corneal Reflex	1.01 (0.43,2.39)	0.984
11-13	Smile	1.17 (0.77,1.77)	0.479
11-14	Palpebral Fissure	1.01 (0.78,1.31)	0.926
11-15	Balance	1.04 (0.78,1.39)	0.799
11-16	Gag Reflex	1.27 (0.56,2.88)	0.580
11-17	Speech	0.85 (0.57,1.26)	0.409
11-18	Tongue Position Relative to Midline	1.59 (0.83,3.06)	0.172
11-19	Shoulder Shrug	0.90 (0.43,1.85)	0.764
11-20	Cranial Nerve Index	0.93 (0.81,1.08)	0.326
11-21	Pinprick	1.13 (0.97,1.32)	0.131
11-22	Light Touch	1.17 (0.96,1.42)	0.129
11-23	Muscle Status	0.98 (0.81,1.20)	0.866
11-27	Babinski Reflex	0.83 (0.56,1.25)	0.373
11-28	Any Symmetric Peripheral Abnormality	1.06 (0.96,1.18)	0.246
11-29	Possible Peripheral Neuropathy	1.06 (0.96,1.18)	0.254
11-30	Probable Peripheral Neuropathy	1.05 (0.89,1.23)	0.550
11-31	Tremor	1.09 (0.92,1.29)	0.318
11-32	Coordination	1.00 (0.80,1.25)	0.989
11-33	Romberg Sign	1.04 (0.78,1.39)	0.799
11-34	Gait	1.06 (0.91,1.25)	0.434
11-35	CNS Index	1.05 (0.93,1.19)	0.458
12-3	Psychoses	1.10 (0.92,1.33)	0.291
12-4	Alcohol Dependence	1.00 (0.83,1.20)	0.997
12-5	Drug Dependence	0.54 (0.23,1.29)	0.178
12-6	Anxiety	1.16 (1.05,1.28)	0.003
12-7	Other Neuroses	1.19 (1.09,1.31)	<0.001
12-8	SCL-90-R Anxiety	1.17 (1.00,1.37)	0.047
12-9	SCL-90-R Depression	1.13 (0.99,1.30)	0.076
12-10	SCL-90-R Hostility	1.18 (0.97,1.42)	0.097
12-11	SCL-90-R Interpersonal Sensitivity	1.07 (0.90,1.26)	0.444
12-12	SCL-90-R Obsessive-compulsive Behavior	1.13 (1.00,1.27)	0.043
12-13	SCL-90-R Paranoid Ideation	1.07 (0.83,1.38)	0.592
12-14	SCL-90-R Phobic Anxiety	1.01 (0.85,1.20)	0.891
12-15	SCL-90-R Psychoticism	1.12 (0.97,1.31)	0.135
12-16	SCL-90-R Somatization	1.17 (1.03,1.33)	0.015
12-17	SCL-90-R Global Severity	1.16 (1.01,1.34)	0.040
12-18	SCL-90-R Positive Symptom Total	1.08 (0.93,1.25)	0.324
12-19	SCL-90-R Positive Symptom Distress Index	1.23 (1.04,1.46)	0.016
13-3	Uncharacterized Hepatitis	1.07 (0.78,1.46)	0.679
13-4	Jaundice	0.60 (0.42,0.85)	0.004
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	1.20 (0.97,1.48)	0.098
13-6	Chronic Liver Disease and Cirrhosis (Nonalcohol-related)	1.15 (0.91,1.45)	0.244
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	1.05 (0.61,1.80)	0.860
13-8	Enlarged Liver	0.93 (0.73,1.19)	0.572
13-9	Other Disorders of the Liver	1.04 (0.95,1.14)	0.354
13-10	Current Hepatomegaly	0.98 (0.69,1.40)	0.913
13-12	AST	1.04 (0.89,1.22)	0.596

Table Ref.	Clinical Parameter	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
13-14	ALT	1.15 (0.97,1.36)	0.112
13-16	GGT	1.02 (0.88,1.18)	0.798
13-18	Alkaline Phosphatase	1.01 (0.86,1.19)	0.861
13-20	Total Bilirubin	0.95 (0.80,1.14)	0.599
13-21	Direct Bilirubin	0.50 (0.21,1.17)	0.124
13-23	LDH	0.94 (0.82,1.08)	0.400
13-25	Cholesterol	0.98 (0.85,1.13)	0.740
13-27	HDL Cholesterol	1.07 (0.95,1.19)	0.271
13-29	Cholesterol-HDL Ratio	1.17 (1.07,1.29)	<0.001
13-31	Triglycerides	1.35 (1.18,1.53)	<0.001
13-33	Creatine Phosphokinase	0.97 (0.83,1.14)	0.743
13-35	Serum Amylase	0.96 (0.73,1.25)	0.755
13-36	Antibodies for Hepatitis A	1.07 (0.98,1.18)	0.137
13-37	Serological Evidence of Prior Hepatitis B Infection	1.26 (1.06,1.50)	0.008
13-38	Antibodies for Hepatitis C	0.65 (0.37,1.15)	0.138
13-39	Stool Hemoccult	1.01 (0.71,1.45)	0.947
13-41	Prealbumin	0.97 (0.71,1.32)	0.834
13-43	Albumin	0.50 (0.29,0.86)	0.015
13-45	α-1-Acid Glycoprotein	1.03 (0.86,1.24)	0.732
13-49	α-2-Macroglobulin	1.05 (0.92,1.19)	0.457
13-51	Apolipoprotein B	1.10 (0.74,1.64)	0.651
13-53	C3 Complement	0.64 (0.41,0.98)	0.038
13-55	C4 Complement	1.03 (0.87,1.22)	0.740
13-57	Haptoglobin	0.98 (0.87,1.12)	0.810
13-59	Transferrin	0.79 (0.64,0.97)	0.021
13-61	Prothrombin Time	0.94 (0.54,1.61)	0.814
14-3	Acne (Lifetime)	1.02 (0.93,1.11)	0.676
14-4	Post-SEA Acne	1.06 (0.96,1.17)	0.251
14-5	Post-SEA Acne (No Pre-SEA Acne)	1.13 (0.98,1.30)	0.086
14-6	Post-SEA Acne (with Pre-SEA Acne)	1.02 (0.87,1.19)	0.802
14-8	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (Excluding Participants with Pre-SEA Acne)	1.13 (0.87,1.47)	0.361
14-10	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (All Post-SEA Occurrences)	1.02 (0.86,1.21)	0.842
14-13	Acneiform Lesions	0.99 (0.82,1.19)	0.920
14-14	Acneiform Scars	0.88 (0.73,1.05)	0.151
14-15	Comedones	0.98 (0.81,1.20)	0.864
14-16	Depigmentation	1.23 (0.91,1.65)	0.182
14-17	Hyperpigmentation	0.99 (0.83,1.18)	0.925
14-18	Inclusion Cysts	1.10 (0.96,1.25)	0.159
14-19	Dermatology Index	1.05 (0.94,1.16)	0.396
15-3	Essential Hypertension	1.18 (1.08,1.29)	<0.001
15-4	Heart Disease (Excluding Essential Hypertension)	0.92 (0.81,1.03)	0.152
15-5	Myocardial Infarction	1.02 (0.88,1.19)	0.750
15-6	Stroke or Transient Ischemic Attack	1.07 (0.85,1.35)	0.545
15-8	Systolic Blood Pressure	0.91 (0.81,1.01)	0.065
15-10	Diastolic Blood Pressure	1.19 (0.98,1.44)	0.078
15-11	Heart Sounds	1.02 (0.86,1.22)	0.801
15-12	Overall ECG	0.94 (0.86,1.03)	0.204

Table Ref.	Clinical Parameter	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
15-13	ECG: RBBB	0.92 (0.74,1.15)	0.472
15-14	ECG: LBBB	0.99 (0.64,1.53)	0.976
15-15	ECG: Nonspecific ST- and T-wave Changes	1.00 (0.90,1.11)	0.971
15-16	ECG: Bradycardia	0.80 (0.65,0.97)	0.024
15-17	ECG: Tachycardia	1.15 (0.58,2.28)	0.686
15-18	ECG: Arrhythmia	0.91 (0.78,1.06)	0.210
15-19	ECG: Evidence of Prior Myocardial Infarction	0.97 (0.79,1.21)	0.815
15-20	Funduscopic Examination	1.10 (0.96,1.27)	0.172
15-21	Carotid Bruits	0.85 (0.61,1.20)	0.355
15-22	Radial Pulses	1.02 (0.85,1.22)	0.871
15-23	Femoral Pulses	0.91 (0.63,1.31)	0.609
15-24	Popliteal Pulses	1.03 (0.76,1.38)	0.864
15-25	Dorsalis Pedis Pulses	1.06 (0.90,1.25)	0.455
15-26	Posterior Tibial Pulses	1.08 (0.87,1.34)	0.482
15-27	Leg Pulses	1.06 (0.91,1.24)	0.464
15-28	Peripheral Pulses	1.06 (0.93,1.21)	0.357
15-30	Resting Pressure Index	1.02 (0.82,1.27)	0.882
15-32	Hyperemic Pressure Index (1 Minute Post-exercise)	1.09 (0.93,1.26)	0.288
15-34	Hyperemic Pressure Index (2 Minutes Post-exercise)	1.05 (0.85,1.30)	0.649
15-35	Intermittent Claudication and Vascular Insufficiency Index	1.09 (0.85,1.42)	0.496
16-13	RBC Morphology	1.02 (0.86,1.22)	0.800
16-16	Absolute Neutrophils (Bands) (Zero vs. Nonzero)	1.04 (0.93,1.17)	0.463
16-20	Absolute Eosinophils (Zero vs. Nonzero)	0.97 (0.84,1.13)	0.739
16-22	Absolute Basophils (Zero vs. Nonzero)	0.98 (0.90,1.08)	0.729
16-24	Fibrinogen	1.03 (0.86,1.24)	0.710
16-26	Erythrocyte Sedimentation Rate	1.09 (0.95,1.24)	0.239
17-3	Occurrence of Kidney Stones	0.94 (0.82,1.08)	0.399
17-4	Occurrence of Past Kidney Disease	1.03 (0.94,1.13)	0.488
17-9	Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero vs. Zero)	1.05 (0.92,1.19)	0.479
17-11	Urinary Occult Blood	0.92 (0.71,1.21)	0.561
17-12	Urinary WBC Count	1.04 (0.88,1.23)	0.677
17-13	Urinary Protein	1.12 (0.88,1.42)	0.347
18-3	Past Thyroid Disease	0.97 (0.84,1.12)	0.709
18-4	Composite Diabetes Indicator (2002 AFHS Diabetes Definition)	1.27 (1.13,1.42)	<0.001
18-5	Composite Diabetes Indicator (Pre-2002 AFHS Diabetes Definition)	1.24 (1.11,1.38)	<0.001
18-8	Time to Diabetes Onset (2002 AFHS Diabetes Definition)	1.25 (1.13,1.38)[b]	<0.001[b]
18-9	Time to Diabetes Onset (Pre-2002 AFHS Diabetes Definition)	1.23 (1.12,1.35)[b]	<0.001[b]
18-10	Thyroid Gland	0.76 (0.49,1.19)	0.229
18-11	Testicular Examination	1.08 (0.91,1.27)	0.375
18-15	Free T$_4$	0.99 (0.84,1.15)	0.864
18-16	Anti-thyroid Antibodies	0.95 (0.51,1.76)	0.872
18-18	Fasting Glucose	1.12 (1.01,1.25)	0.032
18-20	2-hour Postprandial Glucose (Nondiabetics Only)	0.96 (0.85,1.08)	0.470
18-21	2-hour Postprandial Urinary Glucose (Nondiabetics Only)	0.98 (0.87,1.09)	0.660
18-27	Hemoglobin A1c (Diabetics Only)	1.38 (1.08,1.75)	0.005
18-29	C-peptide (Diabetics Only)	0.97 (0.77,1.22)	0.812
18-31	Proinsulin (Diabetics Only)	1.08 (0.88,1.32)	0.474
18-32	GADA (Diabetics Only)	1.62 (0.86,3.07)	0.142
18-34	Total Testosterone	1.09 (0.97,1.22)	0.157

Table G-8. Summary of Unadjusted Results for Dichotomous Variables – Model 4 (Ranch Hands: Log$_2$ (1987 Dioxin)) (Continued)

Table Ref.	Clinical Parameter	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
18-36	Free Testosterone	1.08 (0.90,1.29)	0.421
18-38	Estradiol	0.98 (0.76,1.28)	0.905
18-40	LH	0.92 (0.74,1.15)	0.477
18-42	FSH	0.92 (0.76,1.12)	0.407
19-14	Lupus Panel: ANA Test	1.12 (0.99,1.25)	0.067
19-15	Lupus Panel: Thyroid Microsomal Antibody	1.02 (0.79,1.32)	0.895
19-16	Lupus Panel: MSK Antismooth Muscle Antibody	0.62 (0.40,0.95)	0.029
19-17	Lupus Panel: MSK Antimitochondrial Antibody	0.51 (0.22,1.22)	0.141
19-18	Lupus Panel: MSK Antiparietal Cell Antibody	0.95 (0.70,1.30)	0.750
19-19	Lupus Panel: Rheumatoid Factor	0.92 (0.82,1.02)	0.118
20-3	Asthma	0.92 (0.77,1.10)	0.362
20-4	Bronchitis	1.00 (0.91,1.10)	0.973
20-5	Pneumonia	0.95 (0.83,1.08)	0.436
20-6	Thorax and Lung Abnormality	1.02 (0.92,1.14)	0.658
20-7	X-ray Interpretation	0.93 (0.82,1.05)	0.239
20-9	FVC	1.03 (0.89,1.20)	0.673
20-11	FEV$_1$	1.02 (0.93,1.12)	0.697

[a]Relative risk for a twofold increase in 1987 dioxin.
[b]Hazard ratio, confidence interval, and p-value, based on proportional hazards model, were given for time to diabetes onset variable.

--: Relative risk, confidence interval, and p-value were not presented because of the sparse number of Ranch Hands with abnormalities.

Table G-9. Summary of Unadjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Number (%) Abnormal Ranch Hand	Comparison	Unadjusted Relative Risk (95% C.I.)	p-Value
11-24	Patellar Reflex	Active or Very Active vs. Sluggish or Absent	All	196 (25.5)	309 (26.5)	0.94 (0.77,1.16)	0.592
			Officer	77 (25.2)	130 (28.4)	0.85 (0.61,1.18)	0.327
			Enlisted Flyer	35 (26.3)	52 (28.4)	0.90 (0.54,1.49)	0.680
			Enlisted Groundcrew	84 (25.4)	127 (24.3)	1.06 (0.77,1.46)	0.718
		Sluggish, Active, or Very Active vs. Absent	All	33 (4.3)	35 (3.0)	1.44 (0.89,2.34)	0.139
			Officer	15 (4.9)	15 (3.3)	1.52 (0.73,3.16)	0.260
			Enlisted Flyer	4 (3.0)	5 (2.7)	1.10 (0.29,4.19)	0.885
			Enlisted Groundcrew	14 (4.2)	15 (2.9)	1.50 (0.71,3.14)	0.287
11-25	Achilles Reflex	Active or Very Active vs. Sluggish or Absent	All	463 (60.0)	662 (56.8)	1.14 (0.95,1.37)	0.169
			Officer	202 (66.0)	262 (57.1)	1.46 (1.08,1.97)	0.013
			Enlisted Flyer	84 (63.2)	118 (64.8)	0.93 (0.58,1.48)	0.759
			Enlisted Groundcrew	177 (53.2)	282 (53.8)	0.97 (0.74,1.28)	0.849
		Sluggish, Active, or Very Active vs. Absent	All	186 (24.1)	255 (21.9)	1.13 (0.91,1.41)	0.258
			Officer	81 (26.5)	108 (23.5)	1.17 (0.84,1.63)	0.356
			Enlisted Flyer	37 (27.8)	48 (26.4)	1.08 (0.65,1.78)	0.775
			Enlisted Groundcrew	68 (20.4)	99 (18.9)	1.10 (0.78,1.55)	0.582
11-26	Biceps Reflex	Active or Very Active vs. Sluggish or Absent	All	227 (29.4)	345 (29.5)	0.99 (0.81,1.21)	0.935
			Officer	88 (28.8)	136 (29.5)	0.96 (0.70,1.33)	0.825
			Enlisted Flyer	38 (28.6)	63 (34.4)	0.76 (0.47,1.24)	0.271
			Enlisted Groundcrew	101 (30.2)	146 (27.9)	1.12 (0.83,1.52)	0.453
		Sluggish, Active, or Very Active vs. Absent	All	18 (2.3)	24 (2.1)	1.14 (0.61,2.11)	0.686
			Officer	3 (1.0)	11 (2.4)	0.41 (0.11,1.46)	0.168
			Enlisted Flyer	6 (4.5)	6 (3.3)	1.39 (0.44,4.42)	0.573
			Enlisted Groundcrew	9 (2.7)	7 (1.3)	2.05 (0.75,5.55)	0.160

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
				Ranch Hand	Comparison		
13-47	α-1-Antitrypsin	Abnormal Low vs. Normal	All	8 (1.0)	20 (1.7)	0.61 (0.27,1.39)	0.236
			Officer	6 (2.0)	10 (2.2)	0.90 (0.32,2.51)	0.844
			Enlisted Flyer	0 (0.0)	1 (0.6)	--	0.999[a]
			Enlisted Groundcrew	2 (0.6)	9 (1.8)	0.35 (0.07,1.63)	0.180
		Abnormal High vs. Normal	All	88 (11.5)	114 (9.9)	1.17 (0.87,1.57)	0.292
			Officer	23 (7.5)	34 (7.4)	1.02 (0.59,1.76)	0.952
			Enlisted Flyer	22 (16.5)	23 (12.7)	1.35 (0.72,2.55)	0.349
			Enlisted Groundcrew	43 (13.0)	57 (11.1)	1.19 (0.78,1.81)	0.429
16-4	RBC Count	Abnormal Low vs. Normal	All	56 (7.3)	85 (7.3)	1.00 (0.70,1.42)	0.990
			Officer	32 (10.5)	44 (9.6)	1.11 (0.69,1.80)	0.667
			Enlisted Flyer	9 (6.8)	13 (7.0)	0.94 (0.39,2.27)	0.887
			Enlisted Groundcrew	15 (4.5)	28 (5.3)	0.84 (0.44,1.60)	0.591
		Abnormal High vs. Normal	All	17 (2.2)	29 (2.5)	0.89 (0.48,1.63)	0.700
			Officer	5 (1.6)	5 (1.1)	1.53 (0.44,5.33)	0.506
			Enlisted Flyer	3 (2.3)	8 (4.3)	0.51 (0.13,1.96)	0.325
			Enlisted Groundcrew	9 (2.7)	16 (3.0)	0.88 (0.38,2.02)	0.763
16-6	WBC Count	Abnormal Low vs. Normal	All	74 (9.6)	128 (10.9)	0.86 (0.64,1.17)	0.341
			Officer	31 (10.1)	57 (12.4)	0.79 (0.50,1.26)	0.324
			Enlisted Flyer	19 (14.3)	22 (11.9)	1.26 (0.65,2.45)	0.488
			Enlisted Groundcrew	24 (7.2)	49 (9.3)	0.75 (0.45,1.25)	0.276
		Abnormal High vs. Normal	All	16 (2.1)	26 (2.2)	0.92 (0.49,1.73)	0.793
			Officer	3 (1.0)	7 (1.5)	0.62 (0.16,2.43)	0.497
			Enlisted Flyer	6 (4.5)	5 (2.7)	1.76 (0.52,5.90)	0.363
			Enlisted Groundcrew	7 (2.1)	14 (2.7)	0.77 (0.31,1.93)	0.575

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Number (%) Abnormal Ranch Hand	Comparison	Unadjusted Relative Risk (95% C.I.)	p-Value
16-8	Hemoglobin	Abnormal Low vs. Normal	All	88 (11.4)	135 (11.5)	0.98 (0.74,1.31)	0.904
			Officer	40 (13.1)	63 (13.7)	0.95 (0.62,1.45)	0.809
			Enlisted Flyer	17 (12.8)	19 (10.3)	1.30 (0.65,2.60)	0.467
			Enlisted Groundcrew	31 (9.3)	53 (10.1)	0.90 (0.57,1.44)	0.663
		Abnormal High vs. Normal	All	3 (0.4)	11 (0.9)	0.41 (0.11,1.48)	0.173
			Officer	1 (0.3)	1 (0.2)	1.49 (0.11,20.89)	0.765
			Enlisted Flyer	2 (1.5)	1 (0.5)	2.89 (0.54,15.40)	0.213
			Enlisted Groundcrew	0 (0.0)	9 (1.7)	--	0.039[a]
16-10	Hematocrit	Abnormal Low vs. Normal	All	34 (4.4)	60 (5.1)	0.85 (0.55,1.31)	0.471
			Officer	18 (5.9)	29 (6.3)	0.93 (0.51,1.71)	0.823
			Enlisted Flyer	5 (3.8)	8 (4.3)	0.87 (0.28,2.72)	0.808
			Enlisted Groundcrew	11 (3.3)	23 (4.4)	0.74 (0.36,1.55)	0.428
		Abnormal High vs. Normal	All	6 (0.8)	10 (0.9)	0.90 (0.33,2.50)	0.845
			Officer	2 (0.7)	1 (0.2)	3.01 (0.27,33.32)	0.370
			Enlisted Flyer	2 (1.5)	2 (1.1)	1.39 (0.19,9.99)	0.744
			Enlisted Groundcrew	2 (0.6)	7 (1.3)	0.44 (0.09,2.15)	0.313
16-12	Platelet Count	Abnormal Low vs. Normal	All	12 (1.6)	22 (1.9)	0.82 (0.40,1.67)	0.583
			Officer	9 (3.0)	6 (1.3)	2.30 (0.81,6.52)	0.118
			Enlisted Flyer	1 (0.8)	5 (2.7)	0.27 (0.03,2.35)	0.237
			Enlisted Groundcrew	2 (0.6)	11 (2.1)	0.28 (0.06,1.27)	0.098
		Abnormal High vs. Normal	All	5 (0.6)	14 (1.2)	0.54 (0.19,1.50)	0.234
			Officer	1 (0.3)	2 (0.4)	0.77 (0.07,8.48)	0.828
			Enlisted Flyer	1 (0.8)	1 (0.5)	1.36 (0.08,21.92)	0.829
			Enlisted Groundcrew	3 (0.9)	11 (2.1)	0.42 (0.12,1.51)	0.184
18-6	Diabetic Control (2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	All	24 (3.1)	40 (3.4)	0.89 (0.53,1.50)	0.673
			Officer	10 (3.3)	12 (2.6)	1.25 (0.53,2.93)	0.613
			Enlisted Flyer	6 (4.5)	6 (3.2)	1.37 (0.43,4.35)	0.599
			Enlisted Groundcrew	8 (2.4)	22 (4.2)	0.56 (0.24,1.27)	0.165

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
				Ranch Hand	Comparison		
	Diabetic Control (2002 AFHS Diabetes Definition) (continued)	Diet and Exercise vs. Nondiabetic	All	21 (2.7)	35 (3.0)	0.89 (0.52,1.55)	0.692
			Officer	7 (2.3)	14 (3.0)	0.75 (0.30,1.88)	0.537
			Enlisted Flyer	7 (5.3)	6 (3.2)	1.59 (0.52,4.88)	0.415
			Enlisted Groundcrew	7 (2.1)	15 (2.9)	0.72 (0.29,1.78)	0.472
		Oral Hypoglycemics vs. Nondiabetic	All	75 (9.7)	122 (10.4)	0.92 (0.68,1.24)	0.576
			Officer	25 (8.2)	42 (9.1)	0.89 (0.53,1.50)	0.662
			Enlisted Flyer	13 (9.8)	25 (13.5)	0.71 (0.35,1.45)	0.349
			Enlisted Groundcrew	37 (11.0)	55 (10.5)	1.03 (0.66,1.61)	0.888
		Requiring Insulin vs. Nondiabetic	All	21 (2.7)	29 (2.5)	1.08 (0.61,1.91)	0.792
			Officer	8 (2.6)	11 (2.4)	1.09 (0.43,2.74)	0.858
			Enlisted Flyer	3 (2.3)	6 (3.2)	0.68 (0.17,2.79)	0.595
			Enlisted Groundcrew	10 (3.0)	12 (2.3)	1.28 (0.55,3.00)	0.572
18-7	Diabetic Control (Pre-2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	All	42 (5.4)	73 (6.2)	0.85 (0.58,1.26)	0.430
			Officer	20 (6.5)	18 (3.9)	1.71 (0.89,3.30)	0.109
			Enlisted Flyer	8 (6.0)	14 (7.6)	0.75 (0.30,1.86)	0.535
			Enlisted Groundcrew	14 (4.2)	41 (7.8)	0.51 (0.27,0.96)	0.036
		Diet and Exercise vs. Nondiabetic	All	22 (2.8)	35 (3.0)	0.93 (0.54,1.61)	0.801
			Officer	8 (2.6)	14 (3.0)	0.88 (0.36,2.13)	0.775
			Enlisted Flyer	7 (5.3)	6 (3.2)	1.53 (0.50,4.70)	0.455
			Enlisted Groundcrew	7 (2.1)	15 (2.9)	0.70 (0.28,1.74)	0.441
		Oral Hypoglycemics vs. Nondiabetic	All	75 (9.7)	122 (10.4)	0.91 (0.67,1.24)	0.555
			Officer	25 (8.2)	42 (9.1)	0.92 (0.54,1.54)	0.741
			Enlisted Flyer	13 (9.8)	25 (13.5)	0.68 (0.33,1.40)	0.298
			Enlisted Groundcrew	37 (11.0)	55 (10.5)	1.01 (0.65,1.57)	0.973
		Requiring Insulin vs. Nondiabetic	All	21 (2.7)	29 (2.5)	1.07 (0.61,1.90)	0.805
			Officer	8 (2.6)	11 (2.4)	1.12 (0.44,2.82)	0.811
			Enlisted Flyer	3 (2.3)	6 (3.2)	0.66 (0.16,2.69)	0.559
			Enlisted Groundcrew	10 (3.0)	12 (2.3)	1.25 (0.53,2.93)	0.610

Table G-9. Summary of Unadjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Ranch Hand	Comparison	Unadjusted Relative Risk (95% C.I.)	p-Value
18-13	TSH	Abnormal Low vs. Normal	All	1 (0.1)	7 (0.6)	0.21 (0.03,1.74)	0.149
			Officer	0 (0.0)	3 (0.7)	--	0.405[a]
			Enlisted Flyer	1 (0.8)	1 (0.6)	1.39 (0.11,17.88)	0.799
			Enlisted Groundcrew	0 (0.0)	3 (0.6)	--	0.424[a]
		Abnormal High vs. Normal	All	22 (3.0)	22 (2.0)	1.49 (0.82,2.72)	0.189
			Officer	10 (3.5)	11 (2.6)	1.34 (0.56,3.21)	0.506
			Enlisted Flyer	3 (2.4)	3 (1.7)	1.39 (0.28,7.02)	0.688
			Enlisted Groundcrew	9 (2.8)	8 (1.6)	1.74 (0.66,4.55)	0.261
18-23	Fasting Insulin	Abnormal Low vs. Normal	All	64 (8.2)	116 (9.9)	0.84 (0.61,1.16)	0.290
			Officer	34 (11.1)	52 (11.3)	1.02 (0.64,1.61)	0.947
			Enlisted Flyer	9 (6.8)	15 (8.1)	0.81 (0.34,1.90)	0.621
			Enlisted Groundcrew	21 (6.2)	49 (9.3)	0.67 (0.40,1.15)	0.148
		Abnormal High vs. Normal	All	60 (7.7)	63 (5.4)	1.45 (1.01,2.10)	0.046
			Officer	19 (6.2)	17 (3.7)	1.74 (0.89,3.40)	0.108
			Enlisted Flyer	7 (5.3)	13 (7.0)	0.72 (0.28,1.87)	0.502
			Enlisted Groundcrew	34 (10.1)	33 (6.3)	1.62 (0.98,2.68)	0.059
18-25	2-hour Postprandial Insulin (Nondiabetics Only)	Abnormal Low vs. Normal	All	36 (5.7)	44 (4.7)	1.19 (0.75,1.90)	0.457
			Officer	16 (6.3)	22 (5.8)	1.17 (0.59,2.32)	0.646
			Enlisted Flyer	3 (2.9)	4 (2.9)	0.98 (0.21,4.63)	0.982
			Enlisted Groundcrew	17 (6.2)	18 (4.3)	1.28 (0.63,2.58)	0.495
		Abnormal High vs. Normal	All	305 (48.5)	472 (50.4)	0.94 (0.77,1.16)	0.576
			Officer	114 (44.9)	156 (41.3)	1.18 (0.85,1.64)	0.328
			Enlisted Flyer	57 (55.9)	81 (57.9)	0.92 (0.54,1.56)	0.760
			Enlisted Groundcrew	134 (49.1)	235 (56.2)	0.77 (0.56,1.06)	0.107
20-13	Loss of Vital Capacity	Mild vs. None	All	38 (5.0)	77 (6.6)	0.73 (0.49,1.09)	0.126
			Officer	10 (3.3)	19 (4.1)	0.79 (0.36,1.72)	0.553
			Enlisted Flyer	9 (7.0)	17 (9.3)	0.71 (0.31,1.65)	0.429
			Enlisted Groundcrew	19 (5.7)	41 (7.9)	0.70 (0.40,1.24)	0.222

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)	p-Value
				Ranch Hand	Comparison		
	Loss of Vital Capacity (continued)	Moderate or Severe vs. None	All	14 (1.8)	24 (2.1)	0.86 (0.44,1.68)	0.669
			Officer	6 (2.0)	8 (1.7)	1.12 (0.39,3.28)	0.829
			Enlisted Flyer	1 (0.8)	5 (2.7)	0.27 (0.03,2.33)	0.233
			Enlisted Groundcrew	7 (2.1)	11 (2.1)	0.97 (0.37,2.52)	0.945
20-14	Obstructive Abnormality	Mild vs. None	All	282 (36.9)	406 (35.1)	1.08 (0.88,1.31)	0.464
			Officer	133 (43.8)	188 (41.0)	1.18 (0.87,1.60)	0.282
			Enlisted Flyer	44 (34.1)	78 (43.1)	0.64 (0.39,1.06)	0.083
			Enlisted Groundcrew	105 (31.6)	140 (27.1)	1.20 (0.88,1.63)	0.255
		Moderate vs. None	All	56 (7.3)	93 (8.0)	0.93 (0.65,1.33)	0.701
			Officer	21 (6.9)	26 (5.7)	1.35 (0.73,2.49)	0.336
			Enlisted Flyer	15 (11.6)	23 (12.7)	0.74 (0.36,1.55)	0.428
			Enlisted Groundcrew	20 (6.0)	44 (8.5)	0.73 (0.42,1.27)	0.258
		Severe vs. None	All	23 (3.0)	32 (2.8)	1.11 (0.64,1.93)	0.701
			Officer	10 (3.3)	11 (2.4)	1.52 (0.63,3.67)	0.352
			Enlisted Flyer	6 (4.7)	7 (3.9)	0.98 (0.31,3.06)	0.969
			Enlisted Groundcrew	7 (2.1)	14 (2.7)	0.80 (0.32,2.01)	0.631

[a]P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormalities.

--: Relative risk and confidence interval not presented because of the sparse number of participants with abnormalities.

Table G-10. Summary of Unadjusted Results for Polytomous Variables – Model 2 (Ranch Hands: Log$_2$ (Initial Dioxin))

Table Ref.	Clinical Parameter	Contrast	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
11-24	Patellar Reflex	Active or Very Active vs. Sluggish or Absent	0.96 (0.82,1.13)	0.630
		Sluggish, Active, or Very Active vs. Absent	1.17 (0.87,1.56)	0.305
11-25	Achilles Reflex	Active or Very Active vs. Sluggish or Absent	0.88 (0.76,1.03)	0.107
		Sluggish, Active, or Very Active vs. Absent	0.93 (0.79,1.10)	0.394
11-26	Biceps Reflex	Active or Very Active vs. Sluggish or Absent	0.92 (0.78,1.07)	0.264
		Sluggish, Active, or Very Active vs. Absent	1.38 (0.94,2.02)	0.107
13-47	α-1-Antitrypsin	Abnormal Low vs. Normal	0.74 (0.23,2.42)	0.622
		Abnormal High vs. Normal	0.99 (0.80,1.22)	0.909
16-4	RBC Count	Abnormal Low vs. Normal	0.93 (0.68,1.26)	0.622
		Abnormal High vs. Normal	1.06 (0.65,1.74)	0.807
16-6	WBC Count	Abnormal Low vs. Normal	1.03 (0.79,1.33)	0.834
		Abnormal High vs. Normal	1.01 (0.50,2.04)	0.972
16-8	Hemoglobin	Abnormal Low vs. Normal	0.97 (0.77,1.22)	0.788
		Abnormal High vs. Normal	0.41 (0.04,4.64)	0.472
16-10	Hematocrit	Abnormal Low vs. Normal	1.23 (0.86,1.75)	0.264
		Abnormal High vs. Normal	1.48 (0.69,3.18)	0.319
16-12	Platelet Count	Abnormal Low vs. Normal	0.66 (0.30,1.44)	0.299
		Abnormal High vs. Normal	1.19 (0.44,3.22)	0.726
18-6	Diabetic Control Indicator (2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	0.69 (0.46,1.03)	0.072
		Diet and Exercise vs. Nondiabetic	0.89 (0.56,1.42)	0.636
		Oral Hypoglycemics vs. Nondiabetic	1.09 (0.86,1.37)	0.476
		Requiring Insulin vs. Nondiabetic	1.76 (1.20,2.58)	0.004
18-7	Diabetic Control (Pre-2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	0.89 (0.65,1.21)	0.462
		Diet and Exercise vs. Nondiabetic	0.91 (0.57,1.44)	0.680
		Oral Hypoglycemics vs. Nondiabetic	1.12 (0.89,1.40)	0.352
		Requiring Insulin vs. Nondiabetic	1.79 (1.22,2.62)	0.003
18-13	TSH	Abnormal Low vs. Normal	1.56 (0.44,5.57)	0.493
		Abnormal High vs. Normal	0.92 (0.56,1.51)	0.752
18-23	Fasting Insulin	Abnormal Low vs. Normal	0.79 (0.55,1.14)	0.209
		Abnormal High vs. Normal	1.31 (1.05,1.65)	0.019
18-25	2-hour Postprandial Insulin (Nondiabetics Only)	Abnormal Low vs. Normal	1.16 (0.74,1.80)	0.514
		Abnormal High vs. Normal	1.10 (0.91,1.32)	0.333
20-13	Loss of Vital Capacity	Mild vs. None	0.84 (0.62,1.14)	0.260
		Moderate or Severe vs. None	0.70 (0.39,1.28)	0.250
20-14	Obstructive Abnormality	Mild vs. None	0.82 (0.70,0.97)	0.019
		Moderate vs. None	0.67 (0.49,0.93)	0.016
		Severe vs. None	0.50 (0.28,0.91)	0.022

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk for a twofold increase in initial dioxin.

Table G-11. Summary of Unadjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
11-24	Patellar Reflex	Active or Very Active vs. Sluggish or Absent	Comparison	1,164	309 (26.5)		
			Background RH	349	73 (20.9)	0.80 (0.60,1.08)	0.144
			Low RH	210	65 (31.0)	1.21 (0.88,1.67)	0.248
			High RH	210	58 (27.6)	0.97 (0.69,1.35)	0.855
			Low plus High RH	420	123 (29.3)	1.08 (0.84,1.39)	0.532
		Sluggish, Active, or Very Active vs. Absent	Comparison	1,164	35 (3.0)		
			Background RH	349	9 (2.6)	0.94 (0.44,1.98)	0.867
			Low RH	210	12 (5.7)	1.89 (0.96,3.72)	0.064
			High RH	210	12 (5.7)	1.80 (0.91,3.54)	0.090
			Low plus High RH	420	24 (5.7)	1.84 (1.08,3.15)	0.025
11-25	Achilles Reflex	Active or Very Active vs. Sluggish or Absent	Comparison	1,165	662 (56.8)		
			Background RH	350	206 (58.9)	1.20 (0.94,1.53)	0.149
			Low RH	211	135 (64.0)	1.33 (0.98,1.81)	0.070
			High RH	210	122 (58.1)	0.97 (0.72,1.31)	0.842
			Low plus High RH	421	257 (61.0)	1.14 (0.90,1.43)	0.281
		Sluggish, Active, or Very Active vs. Absent	Comparison	1,165	255 (21.9)		
			Background RH	350	73 (20.9)	1.07 (0.79,1.44)	0.669
			Low RH	211	62 (29.4)	1.45 (1.04,2.02)	0.029
			High RH	210	51 (24.3)	1.03 (0.72,1.46)	0.872
			Low plus High RH	421	113 (26.8)	1.22 (0.94,1.59)	0.133
11-26	Biceps Reflex	Active or Very Active vs. Sluggish or Absent	Comparison	1,168	345 (29.5)		
			Background RH	351	87 (24.8)	0.84 (0.64,1.11)	0.231
			Low RH	211	77 (36.5)	1.35 (0.99,1.84)	0.058
			High RH	210	63 (30.0)	0.96 (0.69,1.33)	0.801
			Low plus High RH	421	140 (33.3)	1.14 (0.89,1.45)	0.294
		Sluggish, Active, or Very Active vs. Absent	Comparison	1,168	24 (2.1)		
			Background RH	351	5 (1.4)	0.73 (0.28,1.95)	0.535
			Low RH	211	5 (2.4)	1.13 (0.43,3.01)	0.803
			High RH	210	8 (3.8)	1.79 (0.79,4.05)	0.166
			Low plus High RH	421	13 (3.1)	1.42 (0.71,2.86)	0.325

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
13-47	α-1-Antitrypsin	Abnormal Low vs. Normal	Comparison	1,154	20	(1.7)		
			Background RH	348	6	(1.7)	0.88 (0.35,2.22)	0.783
			Low RH	208	1	(0.5)	0.30 (0.04,2.22)	0.236
			High RH	211	1	(0.5)	0.31 (0.04,2.33)	0.254
			Low plus High RH	419	2	(0.5)	0.30 (0.07,1.30)	0.109
		Abnormal High vs. Normal	Comparison	1,154	114	(9.9)		
			Background RH	348	28	(8.0)	0.72 (0.47,1.12)	0.145
			Low RH	208	30	(14.4)	1.56 (1.01,2.40)	0.047
			High RH	211	29	(13.7)	1.56 (1.01,2.43)	0.047
			Low plus High RH	419	59	(14.1)	1.56 (1.11,2.19)	0.010
16-4	RBC Count	Abnormal Low vs. Normal	Comparison	1,171	85	(7.3)		
			Background RH	351	31	(8.8)	1.29 (0.84,2.00)	0.245
			Low RH	210	12	(5.7)	0.76 (0.41,1.42)	0.394
			High RH	209	13	(6.2)	0.81 (0.44,1.48)	0.490
			Low plus High RH	419	25	(6.0)	0.78 (0.49,1.25)	0.305
		Abnormal High vs. Normal	Comparison	1,171	29	(2.5)		
			Background RH	351	8	(2.3)	0.95 (0.43,2.12)	0.905
			Low RH	210	5	(2.4)	0.94 (0.36,2.46)	0.898
			High RH	209	4	(1.9)	0.75 (0.26,2.15)	0.589
			Low plus High RH	419	9	(2.1)	0.84 (0.39,1.80)	0.649
16-6	WBC Count	Abnormal Low vs. Normal	Comparison	1,171	128	(10.9)		
			Background RH	351	37	(10.5)	0.91 (0.61,1.34)	0.628
			Low RH	210	17	(8.1)	0.72 (0.42,1.22)	0.216
			High RH	209	20	(9.6)	0.91 (0.55,1.49)	0.696
			Low plus High RH	419	37	(8.8)	0.80 (0.55,1.18)	0.271
		Abnormal High vs. Normal	Comparison	1,171	26	(2.2)		
			Background RH	351	11	(3.1)	1.24 (0.60,2.55)	0.566
			Low RH	210	2	(1.0)	0.42 (0.10,1.77)	0.237
			High RH	209	3	(1.4)	0.72 (0.21,2.40)	0.587
			Low plus High RH	419	5	(1.2)	0.55 (0.20,1.46)	0.228

Table G-11. Summary of Unadjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
16-8	Hemoglobin	Abnormal Low vs. Normal	Comparison	1,171	135 (11.5)		
			Background RH	351	41 (11.7)	1.11 (0.76,1.62)	0.584
			Low RH	210	21 (10.0)	0.82 (0.50,1.34)	0.424
			High RH	209	26 (12.4)	0.99 (0.63,1.56)	0.963
			Low plus High RH	419	47 (11.2)	0.90 (0.63,1.29)	0.564
		Abnormal High vs. Normal	Comparison	1,171	11 (0.9)		
			Background RH	351	2 (0.6)	0.69 (0.15,3.16)	0.632
			Low RH	210	1 (0.5)	0.47 (0.06,3.67)	0.470
			High RH	209	0 (0.0)	--	0.329[c]
			Low plus High RH	419	1 (0.2)	--	0.272[c]
16-10	Hematocrit	Abnormal Low vs. Normal	Comparison	1,171	60 (5.1)		
			Background RH	351	19 (5.4)	1.13 (0.66,1.94)	0.646
			Low RH	210	4 (1.9)	0.35 (0.13,0.97)	0.044
			High RH	209	11 (5.3)	0.97 (0.50,1.88)	0.926
			Low plus High RH	419	15 (3.6)	0.58 (0.31,1.10)	0.096
		Abnormal High vs. Normal	Comparison	1,171	10 (0.9)		
			Background RH	351	3 (0.9)	1.13 (0.30,4.16)	0.859
			Low RH	210	1 (0.5)	0.51 (0.06,4.02)	0.522
			High RH	209	2 (1.0)	1.01 (0.22,4.69)	0.991
			Low plus High RH	419	3 (0.7)	0.72 (0.18,2.80)	0.632
16-12	Platelet Count	Abnormal Low vs. Normal	Comparison	1,168	22 (1.9)		
			Background RH	350	7 (2.0)	1.22 (0.51,2.91)	0.654
			Low RH	210	3 (1.4)	0.70 (0.21,2.37)	0.567
			High RH	209	2 (1.0)	0.44 (0.10,1.89)	0.269
			Low plus High RH	419	5 (1.2)	0.55 (0.20,1.51)	0.247
		Abnormal High vs. Normal	Comparison	1,168	14 (1.2)		
			Background RH	350	3 (0.9)	0.65 (0.19,2.31)	0.509
			Low RH	210	0 (0.0)	--	0.220[c]
			High RH	209	2 (1.0)	0.85 (0.19,3.80)	0.834
			Low plus High RH	419	2 (0.5)	--	0.320[c]

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
18-6	Diabetic Control (2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	Comparison	1,173	40	(3.4)		
			Background RH	352	4	(1.1)	0.38 (0.13,1.08)	0.070
			Low RH	210	13	(6.2)	1.80 (0.93,3.50)	0.081
			High RH	213	7	(3.3)	0.86 (0.37,1.98)	0.725
			Low plus High RH	423	20	(4.7)	1.24 (0.70,2.22)	0.462
		Diet and Exercise vs. Nondiabetic	Comparison	1,173	35	(3.0)		
			Background RH	352	9	(2.6)	0.89 (0.42,1.87)	0.751
			Low RH	210	7	(3.3)	1.15 (0.50,2.63)	0.745
			High RH	213	5	(2.4)	0.77 (0.29,1.99)	0.583
			Low plus High RH	423	12	(2.8)	0.94 (0.48,1.84)	0.848
		Oral Hypoglycemics vs. Nondiabetic	Comparison	1,173	122	(10.4)		
			Background RH	352	22	(6.3)	0.72 (0.44,1.17)	0.185
			Low RH	210	25	(11.9)	1.11 (0.67,1.81)	0.693
			High RH	213	28	(13.2)	1.08 (0.67,1.74)	0.746
			Low plus High RH	423	53	(12.5)	1.09 (0.75,1.59)	0.638
		Requiring Insulin vs. Nondiabetic	Comparison	1,173	29	(2.5)		
			Background RH	352	7	(2.0)	0.89 (0.38,2.06)	0.776
			Low RH	210	2	(1.0)	0.39 (0.09,1.66)	0.201
			High RH	213	12	(5.6)	2.11 (1.04,4.26)	0.037
			Low plus High RH	423	14	(3.3)	0.91 (0.39,2.12)	0.830
18-7	Diabetic Control (Pre-2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	Comparison	1,173	73	(6.2)		
			Background RH	352	13	(3.7)	0.65 (0.35,1.20)	0.172
			Low RH	210	16	(7.6)	1.20 (0.68,2.14)	0.527
			High RH	213	13	(6.1)	0.91 (0.49,1.70)	0.769
			Low plus High RH	423	29	(6.9)	1.05 (0.66,1.66)	0.846
		Diet and Exercise vs. Nondiabetic	Comparison	1,173	35	(3.0)		
			Background RH	352	10	(2.8)	0.99 (0.48,2.04)	0.984
			Low RH	210	7	(3.3)	1.12 (0.49,2.57)	0.791
			High RH	213	5	(2.4)	0.76 (0.29,1.98)	0.577
			Low plus High RH	423	12	(2.8)	0.92 (0.47,1.82)	0.814

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal	Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
	Diabetic Control (Pre-2002 AFHS Diabetes Definition) (continued)	Oral Hypoglycemics vs. Nondiabetic	Comparison	1,173	122 (10.4)		
			Background RH	352	22 (6.3)	0.72 (0.44,1.18)	0.194
			Low RH	210	25 (11.9)	1.06 (0.65,1.75)	0.808
			High RH	213	28 (13.2)	1.08 (0.67,1.74)	0.747
			Low plus High RH	423	53 (12.5)	1.07 (0.74,1.56)	0.712
		Requiring Insulin vs. Nondiabetic	Comparison	1,173	29 (2.5)		
			Background RH	352	7 (2.0)	0.89 (0.38,2.07)	0.785
			Low RH	210	2 (1.0)	0.38 (0.09,1.61)	0.188
			High RH	213	12 (5.6)	2.11 (1.04,4.26)	0.038
			Low plus High RH	423	14 (3.3)	0.90 (0.39,2.09)	0.803
18-13	TSH	Abnormal Low vs. Normal	Comparison	1,089	7 (0.6)		
			Background RH	328	0 (0.0)	--	0.321[c]
			Low RH	201	0 (0.0)	--	0.539[c]
			High RH	203	1 (0.5)	0.76 (0.09,6.25)	0.796
			Low plus High RH	404	1 (0.2)	--	0.600[c]
		Abnormal High vs. Normal	Comparison	1,089	22 (2.0)		
			Background RH	328	12 (3.7)	1.84 (0.89,3.78)	0.098
			Low RH	201	5 (2.5)	1.23 (0.46,3.28)	0.683
			High RH	203	5 (2.5)	1.22 (0.45,3.27)	0.697
			Low plus High RH	404	10 (2.5)	1.22 (0.57,2.61)	0.605
18-23	Fasting Insulin	Abnormal Low vs. Normal	Comparison	1,173	116 (9.9)		
			Background RH	352	38 (10.8)	0.89 (0.59,1.32)	0.549
			Low RH	210	16 (7.6)	0.79 (0.45,1.37)	0.398
			High RH	213	9 (4.2)	0.51 (0.25,1.02)	0.058
			Low plus High RH	423	25 (5.9)	0.63 (0.39,1.01)	0.055
		Abnormal High vs. Normal	Comparison	1,173	63 (5.4)		
			Background RH	352	18 (5.1)	1.16 (0.67,2.02)	0.588
			Low RH	210	17 (8.1)	1.42 (0.80,2.52)	0.233
			High RH	213	25 (11.7)	1.96 (1.18,3.24)	0.009
			Low plus High RH	423	42 (9.9)	1.67 (1.09,2.55)	0.018

Table G-11. Summary of Unadjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
18-25	2-hour Postprandial Insulin (Nondiabetics Only)	Abnormal Low vs. Normal	Comparison	936	44	(4.7)		
			Background RH	308	23	(7.5)	1.38 (0.80,2.36)	0.249
			Low RH	161	5	(3.1)	0.65 (0.25,1.71)	0.385
			High RH	159	8	(5.0)	1.32 (0.59,2.94)	0.501
			Low plus High RH	320	13	(4.1)	0.93 (0.48,1.80)	0.820
		Abnormal High vs. Normal	Comparison	936	472	(50.4)		
			Background RH	308	135	(43.8)	0.88 (0.67,1.16)	0.370
			Low RH	161	83	(51.6)	1.03 (0.73,1.46)	0.875
			High RH	159	87	(54.7)	1.07 (0.75,1.53)	0.703
			Low plus High RH	320	170	(53.1)	1.05 (0.80,1.37)	0.721
20-13	Loss of Vital Capacity	Mild vs. None	Comparison	1,158	77	(6.6)		
			Background RH	347	10	(2.9)	0.47 (0.24,0.92)	0.027
			Low RH	206	16	(7.8)	1.16 (0.66,2.04)	0.607
			High RH	211	12	(5.7)	0.74 (0.39,1.40)	0.353
			Low plus High RH	417	28	(6.7)	0.92 (0.59,1.46)	0.735
		Moderate or Severe vs. None	Comparison	1,158	24	(2.1)		
			Background RH	347	6	(1.7)	1.02 (0.41,2.54)	0.974
			Low RH	206	6	(2.9)	1.29 (0.51,3.28)	0.593
			High RH	211	2	(0.9)	0.33 (0.08,1.47)	0.146
			Low plus High RH	417	8	(1.9)	0.65 (0.26,1.65)	0.366
20-14	Obstructive Abnormality	Mild vs. None	Comparison	1,157	406	(35.1)		
			Background RH	347	140	(40.4)	1.15 (0.89,1.49)	0.289
			Low RH	206	81	(39.3)	1.34 (0.97,1.86)	0.076
			High RH	211	61	(28.9)	0.74 (0.53,1.03)	0.073
			Low plus High RH	417	142	(34.1)	0.99 (0.77,1.27)	0.953
		Moderate vs. None	Comparison	1,157	93	(8.0)		
			Background RH	347	23	(6.6)	0.90 (0.55,1.47)	0.671
			Low RH	206	20	(9.7)	1.41 (0.83,2.40)	0.199
			High RH	211	12	(5.7)	0.59 (0.31,1.11)	0.103
			Low plus High RH	417	32	(7.7)	0.91 (0.59,1.41)	0.675

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Number (%) Abnormal		Unadjusted Relative Risk (95% C.I.)[a,b]	p-Value[a]
	Obstructive Abnormality (continued)	Severe vs. None	Comparison	1,157	32	(2.8)		
			Background RH	347	11	(3.2)	1.24 (0.61,2.52)	0.557
			Low RH	206	10	(4.9)	2.06 (0.98,4.33)	0.056
			High RH	211	2	(1.0)	0.29 (0.07,1.22)	0.092
			Low plus High RH	417	12	(2.9)	0.76 (0.32,1.79)	0.535

[a]Adjusted for body mass index at the time of the blood measurement of dioxin.
[b]Relative risk and confidence interval relative to Comparisons.
[c]P-value determined using a chi-square test with continuity correction because of the sparse number of participants with abnormalities.

--: Relative risk and confidence interval were not presented because of the sparse number of participants with abnormalities.

Note: RH = Ranch Hand.
Background: (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table G-12. Summary of Unadjusted Results for Polytomous Variables – Model 4 (Ranch Hands: Log$_2$ (1987 Dioxin))

Table Ref.	Clinical Parameter	Contrast	Unadjusted Relative Risk (95% C.I.)[a]	p-Value
11-24	Patellar Reflex	Active or Very Active vs. Sluggish or Absent	1.10 (0.99,1.21)	0.069
		Sluggish, Active, or Very Active vs. Absent	1.29 (1.05,1.59)	0.017
11-25	Achilles Reflex	Active or Very Active vs. Sluggish or Absent	0.98 (0.90,1.07)	0.652
		Sluggish, Active, or Very Active vs. Absent	1.05 (0.95,1.17)	0.321
11-26	Biceps Reflex	Active or Very Active vs. Sluggish or Absent	1.08 (0.98,1.19)	0.102
		Sluggish, Active, or Very Active vs. Absent	1.28 (0.97,1.69)	0.082
13-47	α-1-Antitrypsin	Abnormal Low vs. Normal	0.70 (0.44,1.11)	0.129
		Abnormal High vs. Normal	1.10 (0.96,1.27)	0.160
16-4	RBC Count	Abnormal Low vs. Normal	0.88 (0.74,1.05)	0.152
		Abnormal High vs. Normal	1.06 (0.79,1.42)	0.708
16-6	WBC Count	Abnormal Low vs. Normal	0.95 (0.81,1.10)	0.469
		Abnormal High vs. Normal	0.65 (0.47,0.91)	0.011
16-8	Hemoglobin	Abnormal Low vs. Normal	0.99 (0.86,1.14)	0.924
		Abnormal High vs. Normal	0.79 (0.38,1.64)	0.523
16-10	Hematocrit	Abnormal Low vs. Normal	0.94 (0.76,1.17)	0.584
		Abnormal High vs. Normal	1.14 (0.70,1.86)	0.593
16-12	Platelet Count	Abnormal Low vs. Normal	0.80 (0.55,1.16)	0.244
		Abnormal High vs. Normal	0.63 (0.36,1.12)	0.113
18-6	Diabetic Control (2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	1.20 (0.94,1.54)	0.151
		Diet and Exercise vs. Nondiabetic	1.03 (0.78,1.35)	0.851
		Oral Hypoglycemics vs. Nondiabetic	1.32 (1.14,1.53)	<0.001
		Requiring Insulin vs. Nondiabetic	1.43 (1.10,1.85)	0.007
18-7	Diabetic Control (Pre-2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	1.14 (0.94,1.39)	0.174
		Diet and Exercise vs. Nondiabetic	1.00 (0.76,1.31)	0.982
		Oral Hypoglycemics vs. Nondiabetic	1.32 (1.14,1.53)	<0.001
		Requiring Insulin vs. Nondiabetic	1.43 (1.10,1.85)	0.007
18-13	TSH	Abnormal Low vs. Normal	1.92 (0.62,5.94)	0.256
		Abnormal High vs. Normal	0.91 (0.70,1.19)	0.494
18-23	Fasting Insulin	Abnormal Low vs. Normal	0.76 (0.64,0.91)	0.002
		Abnormal High vs. Normal	1.34 (1.14,1.58)	<0.001
18-25	2-hour Postprandial Insulin (Nondiabetics Only)	Abnormal Low vs. Normal	0.91 (0.73,1.15)	0.440
		Abnormal High vs. Normal	1.15 (1.04,1.28)	0.009
20-13	Loss of Vital Capacity	Mild vs. None	1.14 (0.94,1.39)	0.181
		Moderate or Severe vs. None	0.97 (0.70,1.35)	0.871
20-14	Obstructive Abnormality	Mild vs. None	0.88 (0.80,0.97)	0.009
		Moderate vs. None	0.93 (0.78,1.11)	0.433
		Severe vs. None	0.78 (0.59,1.02)	0.070

[a]Relative risk for a twofold increase in 1987 dioxin.

Table G-13. Summary of Adjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adjusted Mean Ranch Hand	Adjusted Mean Comparison	Difference of Adjusted Means (95% C.I.)	p-Value
9-6	Body Mass Index (kg/m²)[a]	All	28.89	28.83	0.05	0.791
		Officer	28.60	28.50	0.10	0.737
		Enlisted Flyer	28.82	29.06	-0.24	0.608
		Enlisted Groundcrew	29.14	29.03	0.12	0.695
10-37	PSA (ng/mL)[a]	All	1.08	1.07	0.01	0.789
		Officer	1.00	1.10	-0.10	0.151
		Enlisted Flyer	1.21	1.07	0.14	0.221
		Enlisted Groundcrew	1.09	1.02	0.07	0.263
12-20	WMS-R: Verbal Paired Associates	All	10.78	10.71	0.07 (-0.21,0.35)	0.622
		Officer	11.72	11.53	0.18 (-0.26,0.63)	0.421
		Enlisted Flyer	10.18	10.38	-0.20 (-0.89,0.50)	0.581
		Enlisted Groundcrew	10.37	10.30	0.07 (-0.36,0.49)	0.753
12-21	WMS-R: Logical Memory, Immediate Recall	All	11.46	11.34	0.12 (-0.16,0.41)	0.397
		Officer	12.50	12.44	0.06 (-0.39,0.51)	0.786
		Enlisted Flyer	10.89	11.13	-0.24 (-0.94,0.46)	0.505
		Enlisted Groundcrew	10.88	10.57	0.31 (-0.12,0.75)	0.153
12-22	WMS-R: Logical Memory, Delayed Recall	All	9.05	8.84	0.20 (-0.11,0.52)	0.197
		Officer	10.15	10.13	0.01 (-0.48,0.51)	0.954
		Enlisted Flyer	8.44	8.55	-0.11 (-0.87,0.66)	0.782
		Enlisted Groundcrew	8.46	7.97	0.50 (0.02,0.97)	0.039
12-23	WMS-R: Visual Reproduction, Immediate Recall	All	27.32	27.17	0.15 (-0.26,0.55)	0.480
		Officer	28.69	28.56	0.13 (-0.50,0.77)	0.680
		Enlisted Flyer	26.22	26.71	-0.49 (-1.48,0.51)	0.337
		Enlisted Groundcrew	26.87	26.47	0.39 (-0.22,1.01)	0.207
12-24	WMS-R: Visual Reproduction, Delayed Recall	All	25.34	25.01	0.33 (-0.20,0.86)	0.221
		Officer	27.03	26.74	0.29 (-0.55,1.13)	0.497
		Enlisted Flyer	24.29	24.63	-0.34 (-1.65,0.97)	0.615
		Enlisted Groundcrew	24.51	23.89	0.62 (-0.19,1.42)	0.132
13-11	AST (U/L)[a]	All	24.78	24.36	0.42	0.237
		Officer	25.72	24.60	1.12	0.053
		Enlisted Flyer	23.82	24.30	-0.48	0.574
		Enlisted Groundcrew	24.51	24.36	0.15	0.785
13-13	ALT (U/L)[a]	All	44.45	44.07	0.38	0.480
		Officer	45.59	44.14	1.45	0.088
		Enlisted Flyer	44.06	44.10	-0.04	0.977
		Enlisted Groundcrew	43.56	44.00	-0.44	0.578
13-15	GGT (U/L)[a]	All	48.31	48.22	0.08	0.941
		Officer	47.59	46.79	0.80	0.645
		Enlisted Flyer	48.34	49.49	-1.15	0.682
		Enlisted Groundcrew	48.56	48.70	-0.14	0.936

Table G-13. Summary of Adjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adjusted Mean Ranch Hand	Adjusted Mean Comparison	Difference of Adjusted Means (95% C.I.)	p-Value
13-17	Alkaline Phosphatase (U/L)[a]	All	94.88	92.74	2.14	0.060
		Officer	90.83	89.65	1.18	0.496
		Enlisted Flyer	96.57	94.54	2.02	0.477
		Enlisted Groundcrew	97.33	94.22	3.11	0.077
13-19	Total Bilirubin (mg/dL)[a]	All	0.493	0.489	0.003	0.754
		Officer	0.507	0.512	-0.004	0.809
		Enlisted Flyer	0.485	0.470	0.016	0.551
		Enlisted Groundcrew	0.490	0.485	0.006	0.731
13-22	LDH (U/L)[a]	All	155.7	153.5	2.2	0.081
		Officer	157.0	153.1	3.9	0.053
		Enlisted Flyer	152.9	152.5	0.3	0.917
		Enlisted Groundcrew	156.6	155.2	1.4	0.468
13-24	Cholesterol (mg/dL)[b]	All	196.3	198.8	-2.5	0.133
		Officer	193.7	197.1	-3.3	0.207
		Enlisted Flyer	199.1	201.5	-2.4	0.558
		Enlisted Groundcrew	196.2	198.0	-1.8	0.478
13-26	HDL Cholesterol (mg/dL)[a]	All	46.56	46.72	-0.17	0.748
		Officer	48.66	48.42	0.25	0.770
		Enlisted Flyer	46.15	45.81	0.35	0.780
		Enlisted Groundcrew	45.10	45.82	-0.72	0.347
13-28	Cholesterol-HDL Ratio[a]	All	4.18	4.21	-0.04	0.482
		Officer	3.95	4.03	-0.09	0.274
		Enlisted Flyer	4.27	4.36	-0.09	0.515
		Enlisted Groundcrew	4.31	4.28	0.03	0.699
13-30	Triglycerides (mg/dL)[a]	All	117.6	116.7	0.9	0.743
		Officer	109.8	108.5	1.3	0.746
		Enlisted Flyer	122.4	124.1	-1.8	0.800
		Enlisted Groundcrew	120.2	118.8	1.4	0.733
13-32	Creatine Phosphokinase (U/L)[a]	All	142.1	139.4	2.7	0.472
		Officer	144.2	142.3	1.9	0.750
		Enlisted Flyer	131.2	138.9	-7.7	0.379
		Enlisted Groundcrew	147.8	140.1	7.6	0.185
13-34	Serum Amylase (U/L)[a]	All	60.07	61.19	-1.12	0.296
		Officer	57.85	61.10	-3.25	0.049
		Enlisted Flyer	59.47	61.66	-2.19	0.404
		Enlisted Groundcrew	62.66	61.30	1.36	0.413
13-40	Prealbumin (mg/dL)[b]	All	29.01	28.76	0.24	0.355
		Officer	29.22	29.00	0.22	0.599
		Enlisted Flyer	29.41	28.60	0.81	0.211
		Enlisted Groundcrew	28.60	28.55	0.05	0.898
13-42	Albumin (mg/dL)	All	4,142.1	4,138.8	3.2 (-21.6,28.1)	0.799
		Officer	4,106.6	4,115.8	-9.2 (-48.4,30.1)	0.648
		Enlisted Flyer	4,176.7	4,157.2	19.4 (-41.7,80.6)	0.534
		Enlisted Groundcrew	4,148.8	4,140.2	8.6 (-29.1,46.3)	0.655

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adjusted Mean		Difference of Adjusted Means (95% C.I.)	p-Value
			Ranch Hand	Comparison		
13-44	α-1-Acid Glycoprotein (mg/dL)[a]	All	77.53	77.37	0.16	0.849
		Officer	74.28	75.41	-1.13	0.388
		Enlisted Flyer	78.53	78.02	0.51	0.810
		Enlisted Groundcrew	80.03	78.73	1.30	0.330
13-46	α-1-Antitrypsin (mg/dL)[b]	All	140.2	139.0	1.2	0.320
		Officer	135.0	134.7	0.3	0.867
		Enlisted Flyer	141.4	142.7	-1.2	0.668
		Enlisted Groundcrew	143.4	140.6	2.9	0.107
13-48	α-2-Macroglobulin (mg/dL)[a]	All	173.4	175.1	-1.7	0.469
		Officer	166.4	164.9	1.6	0.649
		Enlisted Flyer	173.5	181.8	-8.3	0.152
		Enlisted Groundcrew	178.3	180.7	-2.4	0.509
13-50	Apolipoprotein B (mg/dL)[b]	All	102.0	103.0	-0.9	0.392
		Officer	99.3	100.6	-1.3	0.448
		Enlisted Flyer	104.7	105.1	-0.4	0.875
		Enlisted Groundcrew	102.3	103.1	-0.8	0.637
13-52	C3 Complement (mg/dL)[b]	All	121.2	120.5	0.8	0.404
		Officer	116.5	115.2	1.3	0.369
		Enlisted Flyer	122.2	123.1	-0.9	0.694
		Enlisted Groundcrew	124.5	123.6	0.9	0.520
13-54	C4 Complement (mg/dL)[b]	All	24.18	24.49	-0.31	0.248
		Officer	23.56	24.46	-0.91	0.032
		Enlisted Flyer	24.67	24.07	0.60	0.367
		Enlisted Groundcrew	24.65	24.75	-0.10	0.807
13-56	Haptoglobin (mg/dL)[b]	All	123.3	117.3	6.0	0.026
		Officer	109.8	105.0	4.8	0.236
		Enlisted Flyer	126.5	125.5	1.0	0.887
		Enlisted Groundcrew	132.6	123.4	9.1	0.031
13-58	Transferrin (mg/dL)[a]	All	249.1	247.8	1.3	0.469
		Officer	244.4	245.3	-0.9	0.743
		Enlisted Flyer	251.9	248.2	3.7	0.418
		Enlisted Groundcrew	251.9	249.4	2.6	0.359
13-60	Prothrombin Time (seconds)[a]	All	10.76	10.72	0.04	0.131
		Officer	10.77	10.72	0.04	0.325
		Enlisted Flyer	10.75	10.72	0.03	0.703
		Enlisted Groundcrew	10.77	10.72	0.05	0.269
14-11	Duration of Post-SEA Acne (months) (Excluding Participants with Pre-SEA Acne)[b]	All	58.73	46.02	12.72	0.219
		Officer	42.07	27.55	14.52	0.401
		Enlisted Flyer	45.63	84.61	-38.98	0.187
		Enlisted Groundcrew	72.49	48.49	23.99	0.089

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adjusted Mean		Difference of Adjusted Means (95% C.I.)	p-Value
			Ranch Hand	Comparison		
14-12	Duration of Post-SEA Acne (months) (All Post-SEA Occurrences)[b]	All	107.71	115.76	-8.05	0.540
		Officer	101.55	117.63	-16.09	0.511
		Enlisted Flyer	94.45	139.09	-44.65	0.191
		Enlisted Groundcrew	110.86	105.12	5.73	0.739
15-7	Systolic Blood Pressure (mm Hg)[a]	All	129.2	130.4	-1.2	0.129
		Officer	130.1	130.7	-0.6	0.636
		Enlisted Flyer	129.9	131.0	-1.1	0.562
		Enlisted Groundcrew	127.7	129.5	-1.8	0.136
15-9	Diastolic Blood Pressure (mm Hg)[b]	All	75.43	75.55	-0.12	0.789
		Officer	75.15	75.05	0.10	0.888
		Enlisted Flyer	76.01	76.15	-0.14	0.898
		Enlisted Groundcrew	75.13	75.43	-0.30	0.647
15-29	Resting Pressure Index	All	1.217	1.217	0.000 (-0.013,0.013)	0.977
		Officer	1.230	1.234	-0.004 (-0.024,0.016)	0.717
		Enlisted Flyer	1.214	1.219	-0.004 (-0.036,0.027)	0.783
		Enlisted Groundcrew	1.205	1.200	0.006 (-0.014,0.025)	0.575
15-31	Hyperemic Pressure Index (1 Minute Post-exercise)	All	1.137	1.133	0.004 (-0.012,0.020)	0.628
		Officer	1.162	1.157	0.004 (-0.021,0.029)	0.739
		Enlisted Flyer	1.130	1.114	0.016 (-0.023,0.056)	0.412
		Enlisted Groundcrew	1.123	1.124	-0.001 (-0.025,0.023)	0.933
15-33	Hyperemic Pressure Index (2 Minutes Post-exercise)	All	1.197	1.199	-0.002 (-0.016,0.013)	0.805
		Officer	1.221	1.222	-0.001 (-0.024,0.022)	0.945
		Enlisted Flyer	1.196	1.187	0.009 (-0.027,0.045)	0.617
		Enlisted Groundcrew	1.177	1.184	-0.007 (-0.028,0.015)	0.541
16-3	RBC Count (million/mm^3)	All	4.98	4.99	0.00 (-0.05,0.04)	0.856
		Officer	4.92	4.93	-0.01 (-0.08,0.06)	0.765
		Enlisted Flyer	5.01	5.04	-0.03 (-0.13,0.07)	0.597
		Enlisted Groundcrew	5.01	5.00	0.01 (-0.05,0.07)	0.737
16-5	WBC Count (thousand/mm^3)[a]	All	5.91	5.84	0.07	0.359
		Officer	5.71	5.69	0.02	0.883
		Enlisted Flyer	5.92	5.76	0.16	0.375
		Enlisted Groundcrew	6.13	6.05	0.08	0.484
16-7	Hemoglobin (gm/dL)	All	15.01	14.99	0.02 (-0.09,0.12)	0.738
		Officer	14.93	14.91	0.03 (-0.14,0.20)	0.767
		Enlisted Flyer	15.02	15.15	-0.13 (-0.39,0.14)	0.346
		Enlisted Groundcrew	15.02	14.96	0.07 (-0.10,0.23)	0.421
16-9	Hematocrit (percent)	All	45.28	45.22	0.06 (-0.28,0.41)	0.719
		Officer	44.89	44.84	0.05 (-0.50,0.60)	0.857
		Enlisted Flyer	45.39	45.69	-0.30 (-1.14,0.55)	0.489
		Enlisted Groundcrew	45.43	45.22	0.21 (-0.31,0.73)	0.425
16-11	Platelet Count (thousand/mm^3)[b]	All	240.9	237.6	3.3	0.224
		Officer	230.4	237.8	-7.4	0.079
		Enlisted Flyer	249.5	231.1	18.4	0.005
		Enlisted Groundcrew	247.9	240.5	7.4	0.072

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adjusted Mean		Difference of Adjusted Means (95% C.I.)	p-Value
			Ranch Hand	Comparison		
16-14	Absolute Neutrophils (Segs) (thousand/mm^3)[b]	All	3.42	3.38	0.04	0.497
		Officer	3.29	3.25	0.04	0.649
		Enlisted Flyer	3.45	3.36	0.08	0.528
		Enlisted Groundcrew	3.53	3.51	0.02	0.839
16-15	Absolute Neutrophils (Bands) (thousand/mm^3) (Nonzero Measurements)[a]	All	0.150	0.148	0.003	0.665
		Officer	0.147	0.144	0.002	0.799
		Enlisted Flyer	0.158	0.139	0.019	0.225
		Enlisted Groundcrew	0.152	0.156	-0.003	0.736
16-17	Absolute Lymphocytes (thousand/mm^3)[a]	All	1.65	1.65	0.00	0.975
		Officer	1.59	1.60	-0.01	0.825
		Enlisted Flyer	1.60	1.67	-0.06	0.401
		Enlisted Groundcrew	1.73	1.69	0.04	0.438
16-18	Absolute Monocytes (thousand/mm^3)[b]	All	0.414	0.410	0.004	0.691
		Officer	0.410	0.407	0.003	0.835
		Enlisted Flyer	0.411	0.392	0.019	0.412
		Enlisted Groundcrew	0.427	0.428	-0.002	0.919
16-19	Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements)[a]	All	0.156	0.151	0.005	0.394
		Officer	0.144	0.147	-0.003	0.710
		Enlisted Flyer	0.168	0.153	0.016	0.249
		Enlisted Groundcrew	0.160	0.152	0.008	0.350
16-21	Absolute Basophils (thousand/mm^3) (Nonzero Measurements)[a]	All	0.071	0.075	-0.004	0.087
		Officer	0.068	0.074	-0.006	0.061
		Enlisted Flyer	0.072	0.075	-0.003	0.541
		Enlisted Groundcrew	0.074	0.076	-0.001	0.689
16-23	Fibrinogen (mg/dL)[a]	All	363.6	361.5	2.1	0.471
		Officer	354.6	349.5	5.1	0.252
		Enlisted Flyer	360.8	368.4	-7.6	0.279
		Enlisted Groundcrew	372.3	369.4	3.0	0.504
16-25	Erythrocyte Sedimentation Rate (mm/hr)[c]	All	8.42	7.86	0.57	0.109
		Officer	7.41	6.76	0.65	0.186
		Enlisted Flyer	8.54	8.29	0.25	0.777
		Enlisted Groundcrew	9.32	8.73	0.59	0.321
17-5	Blood Urea Nitrogen (mg/dL)[a]	All	15.79	16.12	-0.33	0.113
		Officer	16.04	16.68	-0.64	0.059
		Enlisted Flyer	15.55	15.70	-0.15	0.758
		Enlisted Groundcrew	15.84	15.97	-0.13	0.682
17-6	Serum Creatinine (mg/dL)[a]	All	1.17	1.19	-0.02	0.031
		Officer	1.16	1.20	-0.04	0.010
		Enlisted Flyer	1.17	1.17	0.01	0.754
		Enlisted Groundcrew	1.17	1.19	-0.02	0.306

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adjusted Mean		Difference of Adjusted Means (95% C.I.)	p-Value
			Ranch Hand	Comparison		
17-7	Creatinine Clearance[b]	All	85.44	84.17	1.27	0.136
		Officer	86.13	83.55	2.58	0.059
		Enlisted Flyer	84.06	86.12	-2.06	0.328
		Enlisted Groundcrew	84.99	83.63	1.36	0.289
17-8	Urinary Microalbumin to Urinary Creatinine Ratio (µg/mg) (Nonzero Measurements)[a]	All	27.44	40.13	-12.69	0.037
		Officer	33.37	31.05	2.33	0.822
		Enlisted Flyer	26.21	47.36	-21.15	0.141
		Enlisted Groundcrew	23.85	42.91	-19.06	0.024
17-10	Urine Specific Gravity	All	1.0189	1.0189	0.0000 (-0.0005,0.0006)	0.932
		Officer	1.0182	1.0181	0.0000 (-0.0008,0.0009)	0.920
		Enlisted Flyer	1.0182	1.0195	-0.0013 (-0.0027,0.0001)	0.065
		Enlisted Groundcrew	1.0198	1.0193	0.0005 (-0.0003,0.0014)	0.244
18-12	TSH (µIU/mL)[a]	All	1.653	1.557	0.096	0.024
		Officer	1.778	1.589	0.189	0.009
		Enlisted Flyer	1.516	1.610	-0.094	0.354
		Enlisted Groundcrew	1.611	1.517	0.093	0.132
18-14	Free T_4 (ng/dL)[a]	All	1.081	1.066	0.015	0.056
		Officer	1.072	1.068	0.003	0.788
		Enlisted Flyer	1.115	1.054	0.061	0.002
		Enlisted Groundcrew	1.074	1.065	0.008	0.482
18-17	Fasting Glucose (mg/dL)[a]	All	105.2	105.2	-0.1	0.942
		Officer	104.1	104.5	-0.4	0.778
		Enlisted Flyer	105.0	104.7	0.3	0.906
		Enlisted Groundcrew	106.5	106.4	0.1	0.932
18-19	2-hour Postprandial Glucose (mg/dL) (Nondiabetics Only)[a]	All	111.4	112.8	-1.4	0.454
		Officer	112.3	107.6	4.7	0.096
		Enlisted Flyer	115.2	115.2	0.0	0.999
		Enlisted Groundcrew	107.4	114.8	-7.4	0.006
18-22	Fasting Insulin (µIU/mL)[a]	All	11.10	10.74	0.36	0.160
		Officer	10.73	10.27	0.46	0.242
		Enlisted Flyer	10.83	11.08	-0.25	0.694
		Enlisted Groundcrew	11.53	11.03	0.50	0.212
18-24	2-hour Postprandial Insulin (µIU/mL) (Nondiabetics Only)[a]	All	63.22	64.60	-1.37	0.554
		Officer	60.15	56.97	3.18	0.342
		Enlisted Flyer	69.76	66.38	3.37	0.589
		Enlisted Groundcrew	61.83	69.47	-7.64	0.033
18-26	Hemoglobin A1c (percent) (Diabetics Only)[a]	All	6.95	6.89	0.06	0.674
		Officer	6.69	6.74	-0.05	0.821
		Enlisted Flyer	7.05	6.80	0.25	0.454
		Enlisted Groundcrew	7.14	7.07	0.08	0.732

Table G-13. Summary of Adjusted Results for Continuous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adjusted Mean Ranch Hand	Adjusted Mean Comparison	Difference of Adjusted Means (95% C.I.)	p-Value
18-28	C-peptide (ng/mL) (Diabetics Only)[b]	All	3.41	3.39	0.02	0.892
		Officer	3.49	3.25	0.24	0.406
		Enlisted Flyer	3.27	3.45	-0.18	0.648
		Enlisted Groundcrew	3.45	3.51	-0.06	0.805
18-30	Proinsulin (pmol/L) (Diabetics Only)[a]	All	22.89	22.43	0.46	0.862
		Officer	19.34	19.68	-0.34	0.929
		Enlisted Flyer	25.13	24.44	0.69	0.919
		Enlisted Groundcrew	24.60	23.46	1.14	0.787
18-33	Total Testosterone (ng/dL)[b]	All	416.8	414.6	2.2	0.795
		Officer	405.7	406.4	-0.8	0.954
		Enlisted Flyer	433.5	421.6	11.8	0.569
		Enlisted Groundcrew	414.6	413.4	1.2	0.923
18-35	Free Testosterone (pg/mL)[b]	All	10.47	10.48	-0.01	0.944
		Officer	10.14	10.47	-0.33	0.204
		Enlisted Flyer	10.85	10.39	0.47	0.252
		Enlisted Groundcrew	10.57	10.47	0.10	0.695
18-37	Estradiol (pg/mL) (Measurements Above Sensitivity Limit)[a]	All	23.69	23.30	0.39	0.580
		Officer	23.75	23.25	0.50	0.657
		Enlisted Flyer	23.59	23.86	-0.27	0.873
		Enlisted Groundcrew	23.53	22.99	0.53	0.606
18-39	LH (mIU/mL)[a]	All	4.52	4.33	0.20	0.118
		Officer	4.49	4.09	0.40	0.040
		Enlisted Flyer	4.28	4.36	-0.08	0.787
		Enlisted Groundcrew	4.73	4.61	0.12	0.560
18-41	FSH (mIU/mL)[a]	All	5.64	5.54	0.10	0.557
		Officer	5.80	5.28	0.52	0.053
		Enlisted Flyer	5.17	5.46	-0.29	0.466
		Enlisted Groundcrew	5.85	5.98	-0.13	0.621
19-4	CD3+ Cells (T Cells) (cells/mm^3)[a]	All	1,264.3	1,219.1	45.1	0.231
		Officer	1,271.0	1,202.2	68.8	0.242
		Enlisted Flyer	1,215.3	1,247.1	-31.9	0.722
		Enlisted Groundcrew	1,277.7	1,223.8	53.9	0.359
19-5	CD4+ Cells (Helper T Cells) (cells/mm^3)[b]	All	928.8	906.5	22.3	0.397
		Officer	958.7	917.9	40.7	0.330
		Enlisted Flyer	890.6	919.8	-29.2	0.641
		Enlisted Groundcrew	918.0	892.1	25.9	0.522
19-6	CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]	All	548.7	532.4	16.3	0.426
		Officer	512.1	502.2	9.9	0.742
		Enlisted Flyer	543.3	564.4	-21.1	0.675
		Enlisted Groundcrew	579.7	541.3	38.4	0.242

Table Ref.	Clinical Parameter (Units)	Occupational Category	Adjusted Mean		Difference of Adjusted Means (95% C.I.)	p-Value
			Ranch Hand	Comparison		
19-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]	All	226.4	225.6	0.7	0.938
		Officer	209.7	213.8	-4.1	0.763
		Enlisted Flyer	218.4	239.0	-20.6	0.364
		Enlisted Groundcrew	245.2	230.1	15.1	0.320
19-8	CD20+ Cells (B Cells) (cells/mm^3)[a]	All	190.6	197.1	-6.6	0.489
		Officer	187.9	193.0	-5.1	0.728
		Enlisted Flyer	188.5	201.4	-12.9	0.573
		Enlisted Groundcrew	193.0	198.4	-5.4	0.716
19-9	CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[b]	All	855.7	832.5	23.2	0.356
		Officer	885.3	843.9	41.4	0.299
		Enlisted Flyer	821.7	845.2	-23.6	0.693
		Enlisted Groundcrew	842.7	817.7	25.0	0.517
19-10	Absolute Lymphocytes (cells/mm^3)[a]	All	1,656.8	1,646.0	10.7	0.735
		Officer	1,589.7	1,599.3	-9.6	0.843
		Enlisted Flyer	1,652.8	1,654.1	-1.3	0.987
		Enlisted Groundcrew	1,726.4	1,691.5	34.9	0.479
19-11	IgA (mg/dL)[b]	All	267.5	268.6	-1.1	0.859
		Officer	255.5	256.2	-0.7	0.938
		Enlisted Flyer	265.2	269.3	-4.1	0.786
		Enlisted Groundcrew	281.1	281.4	-0.3	0.975
19-12	IgG (mg/dL)[a]	All	1,146.3	1,163.9	-17.6	0.211
		Officer	1,105.4	1,138.2	-32.8	0.130
		Enlisted Flyer	1,145.3	1,179.9	-34.6	0.325
		Enlisted Groundcrew	1,183.8	1,180.7	3.1	0.885
19-13	IgM (mg/dL)[a]	All	84.42	86.17	-1.75	0.494
		Officer	81.86	83.64	-1.78	0.650
		Enlisted Flyer	80.01	93.83	-13.82	0.031
		Enlisted Groundcrew	87.52	84.86	2.67	0.491
20-8	FVC (percent of predicted)	All	94.93	95.67	-0.74 (-2.14,0.67)	0.303
		Officer	96.12	96.20	-0.08 (-2.31,2.15)	0.945
		Enlisted Flyer	94.12	95.95	-1.83 (-5.30,1.64)	0.301
		Enlisted Groundcrew	94.17	95.10	-0.93 (-3.05,1.19)	0.390
20-10	FEV$_1$ (percent of predicted)	All	84.44	85.28	-0.84 (-2.32,0.65)	0.270
		Officer	85.20	86.49	-1.29 (-3.65,1.06)	0.283
		Enlisted Flyer	83.36	84.71	-1.35 (-5.01,2.31)	0.469
		Enlisted Groundcrew	84.57	84.80	-0.23 (-2.47,2.01)	0.840
20-12	Ratio of Observed FEV$_1$ to Observed FVC[d]	All	0.726	0.727	-0.001	0.698
		Officer	0.720	0.730	-0.010	0.074
		Enlisted Flyer	0.727	0.720	0.007	0.414
		Enlisted Groundcrew	0.733	0.730	0.003	0.537

[a]Means transformed from natural logarithm scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm scale; p-value based on difference of means on natural logarithm scale.

[b]Means transformed from square root scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on square root scale; p-value based on difference of means on square root scale.

[c]Means transformed from natural logarithm (clinical parameter + 0.1) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (clinical parameter + 0.1) scale; p-value based on difference of means on natural logarithm (clinical parameter + 0.1) scale.

[d]Means transformed from natural logarithm (1 – clinical parameter) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (1 – clinical parameter) scale; p-value based on difference of means on natural logarithm (1 – clinical parameter) scale.

Table G-14. Summary of Adjusted Results for Continuous Variables – Model 2 (Ranch Hands: Log$_2$ (Initial Dioxin))

Table Ref.	Clinical Parameter (Units)	R^2	Adjusted Slope (Standard Error)	p-Value
9-6	Body Mass Index (kg/m^2)[a]	0.106	0.007 (0.006)	0.244
10-37	PSA (ng/mL)[a]	0.122	-0.049 (0.033)	0.139
12-20	WMS-R: Verbal Paired Associates	0.085	-0.042 (0.142)	0.767
12-21	WMS-R: Logical Memory, Immediate Recall	0.127	-0.007 (0.142)	0.961
12-22	WMS-R: Logical Memory, Delayed Recall	0.134	-0.007 (0.159)	0.965
12-23	WMS-R: Visual Reproduction, Immediate Recall	0.190	-0.025 (0.203)	0.902
12-24	WMS-R: Visual Reproduction, Delayed Recall	0.221	0.077 (0.254)	0.762
13-11	AST (U/L)[a]	0.095	0.000 (0.014)	0.990
13-13	ALT (U/L)[a]	0.153	0.009 (0.011)	0.390
13-15	GGT (U/L)[a]	0.120	-0.008 (0.022)	0.700
13-17	Alkaline Phosphatase (U/L)[a]	0.041	-0.010 (0.011)	0.368
13-19	Total Bilirubin (mg/dL)[a]	0.075	-0.004 (0.020)	0.844
13-22	LDH (U/L)[a]	0.060	-0.001 (0.008)	0.868
13-24	Cholesterol (mg/dL)[b]	0.082	-0.014 (0.055)	0.797
13-26	HDL Cholesterol (mg/dL)[a]	0.238	-0.007 (0.010)	0.494
13-28	Cholesterol-HDL Ratio[a]	0.153	0.005 (0.012)	0.692
13-30	Triglycerides (mg/dL)[a]	0.082	0.024 (0.024)	0.329
13-32	Creatine Phosphokinase (U/L)[a]	0.127	-0.002 (0.023)	0.931
13-34	Serum Amylase (U/L)[a]	0.117	-0.036 (0.017)	0.031
13-40	Prealbumin (mg/dL)[b]	0.144	-0.046 (0.024)	0.055
13-42	Albumin (mg/dL)	0.081	-18.523 (11.081)	0.095
13-44	α-1-Acid Glycoprotein (mg/dL)[a]	0.150	-0.038 (0.010)	<0.001
13-46	α-1-Antitrypsin (mg/dL)[b]	0.143	-0.048 (0.043)	0.267
13-48	α-2-Macroglobulin (mg/dL)[a]	0.215	-0.002 (0.013)	0.851
13-50	Apolipoprotein B (mg/dL)[b]	0.051	-0.024 (0.049)	0.628
13-52	C3 Complement (mg/dL)[b]	0.173	-0.014 (0.037)	0.707
13-54	C4 Complement (mg/dL)[b]	0.039	-0.053 (0.026)	0.041
13-56	Haptoglobin (mg/dL)[b]	0.129	-0.227 (0.112)	0.043
13-58	Transferrin (mg/dL)[a]	0.028	-0.002 (0.007)	0.752
13-60	Prothrombin Time (seconds)[a]	0.095	0.001 (0.002)	0.750
14-11	Duration of Post-SEA Acne (months) (Excluding Participants with Pre-SEA Acne)[b]	0.349	1.808 (0.455)	<0.001
14-12	Duration of Post-SEA Acne (months) (All Post-SEA Occurrences)[b]	0.087	0.876 (0.474)	0.067
15-7	Systolic Blood Pressure (mm Hg)[a]	0.086	0.002 (0.006)	0.680
15-9	Diastolic Blood Pressure (mm Hg)[b]	0.150	-0.013 (0.023)	0.590
15-29	Resting Pressure Index	0.180	-0.007 (0.007)	0.313
15-31	Hyperemic Pressure Index (1 Minute Post-exercise)	0.190	-0.011 (0.008)	0.179
15-33	Hyperemic Pressure Index (2 Minutes Post-exercise)	0.200	-0.008 (0.007)	0.250
16-3	RBC Count (million/mm^3)	0.083	-0.032 (0.019)	0.090
16-5	WBC Count (thousand/mm^3)[a]	0.183	-0.001 (0.010)	0.901
16-7	Hemoglobin (gm/dL)	0.114	-0.043 (0.049)	0.383
16-9	Hematocrit (percent)	0.098	-0.180 (0.156)	0.250
16-11	Platelet Count (thousand/mm^3)[b]	0.108	0.011 (0.074)	0.881
16-14	Absolute Neutrophils (Segs) (thousand/mm^3)[b]	0.142	-0.013 (0.013)	0.337

Table Ref.	Clinical Parameter (Units)	R^2	Adjusted Slope (Standard Error)	p-Value
16-15	Absolute Neutrophils (Bands) (thousand/mm^3) (Nonzero Measurements)[a]	0.074	-0.064 (0.040)	0.111
16-17	Absolute Lymphocytes (thousand/mm^3)[a]	0.083	0.028 (0.017)	0.092
16-18	Absolute Monocytes (thousand/mm^3)[b]	0.098	0.009 (0.007)	0.174
16-19	Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements)[a]	0.029	-0.021 (0.032)	0.526
16-21	Absolute Basophils (thousand/mm^3) (Nonzero Measurements)[a]	0.048	-0.010 (0.027)	0.708
16-23	Fibrinogen (mg/dL)[a]	0.146	-0.005 (0.007)	0.485
16-25	Erythrocyte Sedimentation Rate (mm/hr)[c]	0.102	0.023 (0.038)	0.537
17-5	Blood Urea Nitrogen (mg/dL)[a]	0.094	0.004 (0.012)	0.715
17-6	Serum Creatinine (mg/dL)[a]	0.078	-0.006 (0.007)	0.392
17-7	Creatinine Clearance[b]	0.493	-0.024 (0.036)	0.509
17-8	Urinary Microalbumin to Urinary Creatinine Ratio (µg/mg) (Nonzero Measurements)[a]	0.376	0.163 (0.156)	0.300
17-10	Urine Specific Gravity	0.057	-0.0002 (0.0003)	0.454
18-12	TSH (µIU/mL)[a]	0.081	0.004 (0.023)	0.853
18-14	Free T$_4$ (ng/dL)[a]	0.040	-0.003 (0.006)	0.598
18-17	Fasting Glucose (mg/dL)[a]	0.125	0.016 (0.009)	0.079
18-19	2-hour Postprandial Glucose (mg/dL) (Nondiabetics Only)[a]	0.137	0.000 (0.017)	0.997
18-22	Fasting Insulin (µIU/mL)[a]	0.322	0.056 (0.023)	0.014
18-24	2-hour Postprandial Insulin (µIU/mL) (Nondiabetics Only)[a]	0.226	0.052 (0.037)	0.163
18-26	Hemoglobin A1c (percent) (Diabetics Only)[a]	0.136	0.015 (0.016)	0.358
18-28	C-peptide (ng/mL) (Diabetics Only)[b]	0.329	-0.091 (0.038)	0.017
18-30	Proinsulin (pmol/L) (Diabetics Only)[a]	0.155	-0.136 (0.100)	0.178
18-33	Total Testosterone (ng/dL)[b]	0.226	0.308 (0.179)	0.086
18-35	Free Testosterone (pg/mL)[b]	0.196	-0.003 (0.023)	0.906
18-37	Estradiol (pg/mL) (Measurements Above Sensitivity Limit)[a]	0.016	-0.001 (0.028)	0.977
18-39	LH (mIU/mL)[a]	0.052	-0.031 (0.025)	0.217
18-41	FSH (mIU/mL)[a]	0.072	-0.030 (0.027)	0.267
19-4	CD3+ Cells (T Cells) (cells/mm^3)[a]	0.135	0.021 (0.032)	0.508
19-5	CD4+ Cells (Helper T Cells) (cells/mm^3)[b]	0.168	0.348 (0.439)	0.429
19-6	CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]	0.029	0.017 (0.035)	0.628
19-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]	0.076	-0.055 (0.044)	0.212
19-8	CD20+ Cells (B Cells) (cells/mm^3)[a]	0.228	0.102 (0.042)	0.016
19-9	CD3+CD4+ Cells (Helper Cells) (cells/mm^3)[b]	0.173	0.350 (0.440)	0.428
19-10	Absolute Lymphocytes (cells/mm^3)[a]	0.085	0.021 (0.017)	0.222
19-11	IgA (mg/dL)[b]	0.051	0.193 (0.169)	0.256
19-12	IgG (mg/dL)[a]	0.098	-0.001 (0.012)	0.928
19-13	IgM (mg/dL)[a]	0.066	-0.013 (0.028)	0.634
20-8	FVC (percent of predicted)	0.136	-0.631 (0.607)	0.299
20-10	FEV$_1$ (percent of predicted)	0.155	0.028 (0.655)	0.966
20-12	Ratio of Observed FEV$_1$ to Observed FVC[d]	0.246	-0.023 (0.011)	0.039

[a]Slope and standard error based on natural logarithm of clinical parameter versus log$_2$ (initial dioxin).
[b]Slope and standard error based on square root of clinical parameter versus log$_2$ (initial dioxin).
[c]Slope and standard error based on natural logarithm of (clinical parameter + 0.1) versus log$_2$ (initial dioxin).
[d]Slope and standard error based on natural logarithm of (1 – clinical parameter) versus log$_2$ (initial dioxin).

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
9-6	Body Mass Index (kg/m^2)[a]	0.063	Comparison	1,168	28.85		
			Background RH	350	27.81	-1.04	<0.001
			Low RH	210	29.72	0.87	0.006
			High RH	211	30.00	1.15	<0.001
			Low plus High RH	421	29.86	1.01	<0.001
10-37	PSA (ng/mL)[a]	0.071	Comparison	1,083	1.07		
			Background RH	323	1.02	-0.05	0.429
			Low RH	187	1.18	0.11	0.159
			High RH	199	1.10	0.03	0.660
			Low plus High RH	386	1.14	0.07	0.256
12-20	WMS-R: Verbal Paired Associates	0.075	Comparison	1,164	10.72		
			Background RH	350	10.79	0.08 (-0.30,0.46)	0.690
			Low RH	210	10.73	0.01 (-0.44,0.47)	0.953
			High RH	207	10.83	0.12 (-0.36,0.59)	0.625
			Low plus High RH	417	10.78	0.07 (-0.29,0.42)	0.715
12-21	WMS-R: Logical Memory, Immediate Recall	0.118	Comparison	1,164	11.33		
			Background RH	350	11.39	0.06 (-0.33,0.44)	0.776
			Low RH	210	11.67	0.33 (-0.13,0.79)	0.158
			High RH	207	11.38	0.05 (-0.43,0.53)	0.844
			Low plus High RH	417	11.52	0.19 (-0.16,0.55)	0.291
12-22	WMS-R: Logical Memory, Delayed Recall	0.135	Comparison	1,163	8.85		
			Background RH	350	8.96	0.11 (-0.31,0.53)	0.612
			Low RH	210	9.18	0.33 (-0.17,0.84)	0.195
			High RH	207	9.12	0.27 (-0.25,0.79)	0.311
			Low plus High RH	417	9.15	0.30 (-0.09,0.69)	0.127
12-23	WMS-R: Visual Reproduction, Immediate Recall	0.164	Comparison	1,132	27.20		
			Background RH	342	27.31	0.12 (-0.42,0.66)	0.676
			Low RH	201	27.43	0.23 (-0.43,0.89)	0.487
			High RH	205	27.33	0.14 (-0.54,0.81)	0.688
			Low plus High RH	406	27.38	0.19 (-0.32,0.69)	0.470
12-24	WMS-R: Visual Reproduction, Delayed Recall	0.179	Comparison	1,132	25.03		
			Background RH	342	25.32	0.30 (-0.41,1.01)	0.413
			Low RH	201	25.53	0.50 (-0.36,1.37)	0.256
			High RH	205	25.28	0.26 (-0.63,1.14)	0.573
			Low plus High RH	406	25.40	0.38 (-0.28,1.04)	0.263
13-11	AST (U/L)[a]	0.043	Comparison	1,149	24.39		
			Background RH	346	24.65	0.26	0.582
			Low RH	207	25.11	0.72	0.217
			High RH	209	24.58	0.19	0.740
			Low plus High RH	416	24.84	0.45	0.305

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
13-13	ALT (U/L)[a]	0.121	Comparison	1,149	44.17		
			Background RH	346	44.14	-0.03	0.971
			Low RH	207	45.04	0.87	0.310
			High RH	209	44.34	0.17	0.843
			Low plus High RH	416	44.69	0.52	0.427
13-15	GGT (U/L)[a]	0.110	Comparison	1,149	48.25		
			Background RH	346	46.75	-1.50	0.311
			Low RH	207	50.42	2.17	0.246
			High RH	209	48.73	0.48	0.801
			Low plus High RH	416	49.56	1.31	0.355
13-17	Alkaline Phosphatase (U/L)[a]	0.036	Comparison	1,150	92.67		
			Background RH	347	95.06	2.39	0.117
			Low RH	207	95.81	3.14	0.092
			High RH	211	93.24	0.57	0.758
			Low plus High RH	418	94.51	1.84	0.193
13-19	Total Bilirubin (mg/dL)[a]	0.040	Comparison	1,149	0.488		
			Background RH	346	0.493	0.005	0.729
			Low RH	207	0.501	0.013	0.464
			High RH	209	0.481	-0.007	0.709
			Low plus High RH	416	0.491	0.003	0.821
13-22	LDH (U/L)[a]	0.054	Comparison	1,149	153.6		
			Background RH	346	156.4	2.8	0.103
			Low RH	207	155.5	1.9	0.346
			High RH	209	154.7	1.1	0.608
			Low plus High RH	416	155.1	1.5	0.337
13-24	Cholesterol (mg/dL)[b]	0.071	Comparison	1,149	199.1		
			Background RH	346	196.4	-2.7	0.230
			Low RH	207	197.2	-1.9	0.499
			High RH	209	195.1	-4.0	0.148
			Low plus High RH	416	196.2	-2.9	0.158
13-26	HDL Cholesterol (mg/dL)[a]	0.207	Comparison	1,149	46.69		
			Background RH	346	46.78	0.09	0.894
			Low RH	207	46.91	0.22	0.785
			High RH	209	45.62	-1.07	0.209
			Low plus High RH	416	46.26	-0.43	0.504
13-28	Cholesterol-HDL Ratio[a]	0.141	Comparison	1,149	4.22		
			Background RH	346	4.16	-0.06	0.359
			Low RH	207	4.17	-0.05	0.513
			High RH	209	4.23	0.01	0.889
			Low plus High RH	416	4.20	-0.02	0.740
13-30	Triglycerides (mg/dL)[a]	0.106	Comparison	1,149	117.0		
			Background RH	346	113.6	-3.4	0.344
			Low RH	207	120.8	3.8	0.402
			High RH	209	121.7	4.7	0.308
			Low plus High RH	416	121.3	4.3	0.218

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
13-32	Creatine Phosphokinase (U/L)[a]	0.129	Comparison	1,149	139.8		
			Background RH	346	141.4	1.6	0.733
			Low RH	207	141.5	1.7	0.767
			High RH	209	145.0	5.2	0.403
			Low plus High RH	416	143.3	3.5	0.450
13-34	Serum Amylase (U/L)[a]	0.072	Comparison	1,149	61.20		
			Background RH	346	60.00	-1.20	0.404
			Low RH	207	61.16	-0.04	0.984
			High RH	209	58.76	-2.44	0.166
			Low plus High RH	416	59.94	-1.26	0.344
13-40	Prealbumin (mg/dL)[b]	0.064	Comparison	1,149	28.77		
			Background RH	346	28.89	0.12	0.733
			Low RH	207	29.43	0.66	0.127
			High RH	209	28.77	0.00	0.997
			Low plus High RH	416	29.09	0.32	0.321
13-42	Albumin (mg/dL)	0.041	Comparison	1,149	4,138.1		
			Background RH	346	4,133.5	-4.6 (-38.0,28.7)	0.786
			Low RH	207	4,165.0	26.9 (-13.6,67.4)	0.193
			High RH	209	4,131.3	-6.8 (-48.3,34.7)	0.748
			Low plus High RH	416	4,148.1	10.0 (-21.0,40.9)	0.528
13-44	α-1-Acid Glycoprotein (mg/dL)[a]	0.047	Comparison	1,149	77.30		
			Background RH	346	76.76	-0.54	0.634
			Low RH	207	79.45	2.15	0.128
			High RH	209	76.44	-0.86	0.544
			Low plus High RH	416	77.92	0.62	0.561
13-46	α-1-Antitrypsin (mg/dL)[b]	0.098	Comparison	1,149	138.9		
			Background RH	346	139.3	0.4	0.803
			Low RH	207	141.9	3.0	0.114
			High RH	209	139.5	0.6	0.734
			Low plus High RH	416	140.7	1.8	0.208
13-48	α-2-Macro-globulin (mg/dL)[a]	0.175	Comparison	1,149	174.2		
			Background RH	346	174.2	0.0	0.986
			Low RH	207	176.0	1.8	0.628
			High RH	209	168.6	-5.6	0.133
			Low plus High RH	416	172.2	-2.0	0.486
13-50	Apolipoprotein B (mg/dL)[b]	0.044	Comparison	1,149	103.1		
			Background RH	346	102.0	-1.1	0.484
			Low RH	207	102.8	-0.3	0.864
			High RH	209	101.1	-2.0	0.278
			Low plus High RH	416	101.9	-1.2	0.400
13-52	C3 Complement (mg/dL)[b]	0.178	Comparison	1,149	120.4		
			Background RH	346	120.1	-0.3	0.835
			Low RH	207	124.2	3.8	0.011
			High RH	209	119.9	-0.5	0.738
			Low plus High RH	416	122.0	1.6	0.154

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
13-54	C4 Complement (mg/dL)[b]	0.052	Comparison	1,149	24.47		
			Background RH	346	24.11	-0.36	0.325
			Low RH	207	24.69	0.22	0.611
			High RH	209	23.69	-0.78	0.085
			Low plus High RH	416	24.19	-0.28	0.408
13-56	Haptoglobin (mg/dL)[b]	0.081	Comparison	1,149	117.3		
			Background RH	346	122.1	4.8	0.187
			Low RH	207	125.2	7.9	0.073
			High RH	209	123.2	5.9	0.186
			Low plus High RH	416	124.2	6.9	0.040
13-58	Transferrin (mg/dL)[a]	0.028	Comparison	1,149	247.6		
			Background RH	346	245.4	-2.2	0.360
			Low RH	207	254.3	6.7	0.027
			High RH	209	249.8	2.2	0.471
			Low plus High RH	416	252.0	4.4	0.055
13-60	Prothrombin Time (seconds)[a]	0.028	Comparison	892	10.72		
			Background RH	268	10.79	0.07	0.042
			Low RH	144	10.75	0.03	0.400
			High RH	156	10.72	0.00	0.999
			Low plus High RH	300	10.73	0.01	0.592
14-11	Duration of Post-SEA Acne (months) (Excluding Participants with Pre-SEA Acne)[b]	0.100	Comparison	86	49.97		
			Background RH	32	47.66	-2.31	0.867
			Low RH	26	43.16	-6.81	0.637
			High RH	30	104.25	54.28	0.002
			Low plus High RH	56	72.59	22.62	0.075
14-12	Duration of Post-SEA Acne (months) (All Post-SEA Occurrences)[b]	0.020	Comparison	231	117.84		
			Background RH	83	109.81	-8.03	0.653
			Low RH	57	86.91	-30.93	0.109
			High RH	61	132.72	14.88	0.487
			Low plus High RH	118	109.39	-8.45	0.590
15-7	Systolic Blood Pressure (mm Hg)[a]	0.059	Comparison	1,146	130.5		
			Background RH	344	130.5	0.0	0.980
			Low RH	202	127.6	-2.9	0.025
			High RH	209	128.9	-1.6	0.214
			Low plus High RH	411	128.2	-2.3	0.022
15-9	Diastolic Blood Pressure (mm Hg)[b]	0.119	Comparison	1,146	75.57		
			Background RH	344	75.55	-0.02	0.966
			Low RH	202	75.36	-0.21	0.767
			High RH	209	75.28	-0.29	0.688
			Low plus High RH	411	75.32	-0.25	0.643

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)		p-Value
15-29	Resting Pressure Index	0.138	Comparison	1,112	1.217			
			Background RH	336	1.209	-0.008	(-0.025,0.009)	0.358
			Low RH	192	1.231	0.014	(-0.007,0.035)	0.203
			High RH	203	1.218	0.001	(-0.020,0.023)	0.897
			Low plus High RH	395	1.224	0.007	(-0.009,0.023)	0.365
15-31	Hyperemic Pressure Index (1 Minute Post-exercise)	0.176	Comparison	1,100	1.131			
			Background RH	336	1.127	-0.004	(-0.025,0.017)	0.709
			Low RH	195	1.153	0.021	(-0.005,0.047)	0.108
			High RH	197	1.135	0.004	(-0.023,0.030)	0.784
			Low plus High RH	392	1.144	0.012	(-0.007,0.032)	0.219
15-33	Hyperemic Pressure Index (2 Minutes Post-exercise)	0.171	Comparison	1,102	1.198			
			Background RH	336	1.189	-0.009	(-0.028,0.011)	0.379
			Low RH	195	1.207	0.010	(-0.014,0.033)	0.419
			High RH	197	1.198	0.001	(-0.023,0.025)	0.956
			Low plus High RH	392	1.203	0.005	(-0.013,0.023)	0.574
16-3	RBC Count (million/mm^3)	0.083	Comparison	1,168	4.99			
			Background RH	350	5.00	0.01	(-0.04,0.07)	0.670
			Low RH	210	5.00	0.02	(-0.05,0.09)	0.597
			High RH	209	4.92	-0.07	(-0.13,0.00)	0.062
			Low plus High RH	419	4.96	-0.02	(-0.08,0.03)	0.365
16-5	WBC Count (thousand/mm^3)[a]	0.122	Comparison	1,168	5.84			
			Background RH	350	5.94	0.10		0.324
			Low RH	210	5.91	0.07		0.534
			High RH	209	5.83	-0.01		0.913
			Low plus High RH	419	5.87	0.03		0.739
16-7	Hemoglobin (gm/dL)	0.094	Comparison	1,168	14.99			
			Background RH	350	15.00	0.01 (-0.13,0.15)		0.895
			Low RH	210	15.07	0.08 (-0.09,0.25)		0.355
			High RH	209	14.92	-0.08 (-0.25,0.10)		0.404
			Low plus High RH	419	15.00	0.00 (-0.13,0.14)		0.964
16-9	Hematocrit (percent)	0.074	Comparison	1,168	45.22			
			Background RH	350	45.30	0.08 (-0.38,0.54)		0.721
			Low RH	210	45.45	0.23 (-0.33,0.79)		0.417
			High RH	209	44.94	-0.28 (-0.86,0.29)		0.332
			Low plus High RH	419	45.19	-0.03 (-0.45,0.40)		0.904
16-11	Platelet Count (thousand/mm^3)[b]	0.052	Comparison	1,165	238.0			
			Background RH	349	237.9	-0.1		0.982
			Low RH	210	240.2	2.2		0.604
			High RH	209	246.8	8.8		0.051
			Low plus High RH	419	243.5	5.5		0.099
16-14	Absolute Neutrophils (Segs) (thousand/mm^3)[b]	0.105	Comparison	1,168	3.37			
			Background RH	350	3.40	0.03		0.694
			Low RH	210	3.50	0.13		0.153
			High RH	209	3.34	-0.03		0.702
			Low plus High RH	419	3.42	0.05		0.499

Table G-15. Summary of Adjusted Results for Continuous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
16-15	Absolute Neutrophils (Bands) (thousand/mm^3) (Nonzero Measurements)[a]	0.035	Comparison	931	0.147		
			Background RH	290	0.144	-0.003	0.722
			Low RH	163	0.159	0.012	0.272
			High RH	171	0.151	0.004	0.699
			Low plus High RH	334	0.155	0.008	0.331
16-17	Absolute Lymphocytes (thousand/mm^3)[a]	0.050	Comparison	1,168	1.65		
			Background RH	350	1.66	0.01	0.798
			Low RH	210	1.59	-0.06	0.195
			High RH	209	1.68	0.03	0.592
			Low plus High RH	419	1.63	-0.02	0.626
16-18	Absolute Monocytes (thousand/mm^3)[b]	0.046	Comparison	1,168	0.411		
			Background RH	350	0.426	0.015	0.250
			Low RH	210	0.403	-0.008	0.607
			High RH	209	0.403	-0.008	0.632
			Low plus High RH	419	0.403	-0.008	0.511
16-19	Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements)[a]	0.028	Comparison	1,042	0.151		
			Background RH	319	0.160	0.009	0.227
			Low RH	185	0.158	0.007	0.402
			High RH	193	0.144	-0.007	0.427
			Low plus High RH	378	0.151	0.000	0.999
16-21	Absolute Basophils (thousand/mm^3) (Nonzero Measurements)[a]	0.029	Comparison	617	0.075		
			Background RH	181	0.070	-0.005	0.051
			Low RH	108	0.073	-0.002	0.520
			High RH	108	0.073	-0.002	0.502
			Low plus High RH	216	0.073	-0.002	0.384
16-23	Fibrinogen (mg/dL)[a]	0.093	Comparison	1,168	361.0		
			Background RH	349	362.1	1.1	0.771
			Low RH	210	368.3	7.3	0.119
			High RH	209	360.7	-0.3	0.948
			Low plus High RH	419	364.5	3.5	0.329
16-25	Erythrocyte Sedimentation Rate (mm/hr)[c]	0.071	Comparison	1,168	7.81		
			Background RH	350	8.02	0.21	0.650
			Low RH	210	8.92	1.11	0.060
			High RH	209	8.69	0.88	0.143
			Low plus High RH	419	8.80	0.99	0.027
17-5	Blood Urea Nitrogen (mg/dL)[a]	0.084	Comparison	1,174	16.06		
			Background RH	352	15.73	-0.33	0.239
			Low RH	211	15.65	-0.41	0.223
			High RH	213	15.95	-0.11	0.749
			Low plus High RH	424	15.80	-0.26	0.313

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Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
17-6	Serum Creatinine (mg/dL)[a]	0.067	Comparison	1,174	1.18		
			Background RH	352	1.16	-0.02	0.999
			Low RH	211	1.17	-0.01	0.503
			High RH	213	1.16	-0.02	0.093
			Low plus High RH	424	1.17	-0.01	0.117
17-7	Creatinine Clearance[b]	0.473	Comparison	1,174	82.35		
			Background RH	351	83.19	0.84	0.394
			Low RH	211	85.27	2.92	0.015
			High RH	213	83.97	1.62	0.188
			Low plus High RH	424	84.61	2.26	0.014
17-8	Urinary Micro-albumin to Urinary Creatinine Ratio (µg/mg) (Nonzero Measurements)[a]	0.260	Comparison	141	38.47		
			Background RH	42	29.42	-9.05	0.284
			Low RH	35	22.00	-16.47	0.033
			High RH	29	30.19	-8.28	0.412
			Low plus High RH	64	25.39	-13.08	0.051
17-10	Urine Specific Gravity	0.040	Comparison	1,174	1.0188		
			Background RH	352	1.0189	0.0001 (-0.0006,0.0009)	0.782
			Low RH	211	1.0191	0.0003 (-0.0006,0.0012)	0.544
			High RH	213	1.0185	-0.0003 (-0.0012,0.0007)	0.575
			Low plus High RH	424	1.0188	0.0000 (-0.0007,0.0007)	0.987
18-12	TSH (µIU/mL)[a]	0.031	Comparison	1,089	1.560		
			Background RH	327	1.682	0.122	0.036
			Low RH	201	1.614	0.054	0.422
			High RH	203	1.656	0.096	0.172
			Low plus High RH	404	1.635	0.075	0.150
18-14	Free T_4 (ng/dL)[a]	0.017	Comparison	1,089	1.066		
			Background RH	327	1.080	0.014	0.191
			Low RH	201	1.080	0.014	0.271
			High RH	203	1.085	0.019	0.145
			Low plus High RH	404	1.083	0.017	0.090
18-17	Fasting Glucose (mg/dL)[a]	0.133	Comparison	1,162	105.0		
			Background RH	349	105.4	0.4	0.781
			Low RH	206	105.1	0.1	0.984
			High RH	211	105.4	0.4	0.792
			Low plus High RH	417	105.3	0.3	0.848
18-19	2-hour Postprandial Glucose (mg/dL) (Nondiabetics Only)[a]	0.122	Comparison	931	112.7		
			Background RH	305	113.3	0.6	0.794
			Low RH	158	109.6	-3.1	0.298
			High RH	159	108.3	-4.4	0.153
			Low plus High RH	317	108.9	-3.8	0.100

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
18-22	Fasting Insulin (μIU/mL)[a]	0.263	Comparison	1,162	10.77		
			Background RH	349	11.07	0.30	0.379
			Low RH	206	11.03	0.26	0.528
			High RH	211	11.27	0.50	0.247
			Low plus High RH	417	11.15	0.38	0.233
18-24	2-hour Postprandial Insulin (μIU/mL) (Nondiabetics Only)[a]	0.201	Comparison	931	64.52		
			Background RH	305	64.00	-0.52	0.864
			Low RH	158	61.27	-3.25	0.392
			High RH	159	61.06	-3.46	0.376
			Low plus High RH	317	61.16	-3.36	0.248
18-26	Hemoglobin A1c (percent) (Diabetics Only)[a]	0.073	Comparison	215	6.89		
			Background RH	42	6.78	-0.11	0.626
			Low RH	45	6.99	0.10	0.649
			High RH	49	7.05	0.16	0.440
			Low plus High RH	94	7.02	0.13	0.415
18-28	C-peptide (ng/mL) (Diabetics Only)[b]	0.209	Comparison	215	3.38		
			Background RH	42	3.39	0.01	0.955
			Low RH	45	3.76	0.38	0.158
			High RH	49	3.10	-0.28	0.271
			Low plus High RH	94	3.41	0.03	0.868
18-30	Proinsulin (pmol/L) (Diabetics Only)[a]	0.170	Comparison	215	22.44		
			Background RH	42	20.50	-1.94	0.628
			Low RH	45	24.34	1.90	0.654
			High RH	49	23.81	1.37	0.733
			Low plus High RH	94	24.06	1.62	0.604
18-33	Total Testosterone (ng/dL)[b]	0.158	Comparison	1,161	414.2		
			Background RH	348	416.3	2.1	0.852
			Low RH	210	415.6	1.4	0.922
			High RH	210	417.1	2.9	0.840
			Low plus High RH	420	416.3	2.1	0.842
18-35	Free Testosterone (pg/mL)[b]	0.169	Comparison	1,161	10.47		
			Background RH	348	10.26	-0.21	0.332
			Low RH	210	10.75	0.28	0.306
			High RH	210	10.44	-0.03	0.910
			Low plus High RH	420	10.59	0.12	0.554
18-37	Estradiol (pg/mL) (Measurements Above Sensitivity Limit)[a]	0.009	Comparison	746	23.38		
			Background RH	221	24.13	0.85	0.370
			Low RH	139	23.24	-0.04	0.968
			High RH	142	23.28	0.00	0.999
			Low plus High RH	281	23.26	-0.02	0.980

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
18-39	LH (mIU/mL)[a]	0.055	Comparison	1,161	4.30		
			Background RH	348	4.51	0.21	0.208
			Low RH	210	4.81	0.51	0.015
			High RH	210	4.20	-0.10	0.614
			Low plus High RH	420	4.49	0.19	0.213
18-41	FSH (mIU/mL)[a]	0.077	Comparison	1,161	5.51		
			Background RH	348	5.57	0.06	0.791
			Low RH	210	6.05	0.54	0.061
			High RH	210	5.29	-0.22	0.431
			Low plus High RH	420	5.66	0.15	0.488
19-4	CD3+ Cells (T Cells) (cells/mm^3)[a]	0.079	Comparison	418	1,223.1		
			Background RH	122	1,225.4	2.3	0.965
			Low RH	72	1,290.9	67.8	0.285
			High RH	78	1,309.9	86.8	0.167
			Low plus High RH	150	1,300.8	77.7	0.102
19-5	CD4+ Cells (Helper T Cells) (cells/mm^3)[b]	0.098	Comparison	418	910.7		
			Background RH	122	892.3	-18.4	0.612
			Low RH	72	950.2	39.5	0.369
			High RH	78	976.3	65.6	0.133
			Low plus High RH	150	963.8	53.1	0.108
19-6	CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]	0.040	Comparison	418	532.7		
			Background RH	122	544.3	11.6	0.683
			Low RH	72	552.0	19.3	0.572
			High RH	78	550.8	18.1	0.590
			Low plus High RH	150	551.4	18.7	0.463
19-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]	0.042	Comparison	418	225.3		
			Background RH	122	222.1	-3.2	0.804
			Low RH	72	238.2	12.9	0.417
			High RH	78	219.7	-5.6	0.712
			Low plus High RH	150	228.4	3.1	0.788
19-8	CD20+ Cells (B Cells) (cells/mm^3)[a]	0.118	Comparison	418	198.5		
			Background RH	122	191.1	-7.4	0.572
			Low RH	72	173.1	-25.4	0.090
			High RH	78	209.6	11.1	0.494
			Low plus High RH	150	191.2	-7.3	0.534
19-9	CD3+CD4+ Cells (Helper T Cells) (cells/mm^3)[b]	0.104	Comparison	418	836.6		
			Background RH	122	823.8	-12.8	0.710
			Low RH	72	868.9	32.3	0.441
			High RH	78	904.1	67.5	0.106
			Low plus High RH	150	887.1	50.5	0.108

Table Ref.	Clinical Parameter (Units)	R^2	Dioxin Category	n	Adjusted Mean	Difference of Adjusted Mean vs. Comparisons (95% C.I.)	p-Value
19-10	Absolute Lymphocytes (cells/mm^3)[a]	0.059	Comparison	1,064	1,650.6		
			Background RH	315	1,643.6	-7.0	0.870
			Low RH	187	1,639.2	-11.4	0.825
			High RH	189	1,691.7	41.1	0.441
			Low plus High RH	376	1,665.4	14.8	0.708
19-11	IgA (mg/dL)[b]	0.031	Comparison	1,064	267.5		
			Background RH	315	263.7	-3.8	0.642
			Low RH	187	276.1	8.6	0.382
			High RH	189	263.3	-4.2	0.675
			Low plus High RH	376	269.6	2.1	0.774
19-12	IgG (mg/dL)[a]	0.064	Comparison	1,064	1,163.0		
			Background RH	315	1,139.0	-24.0	0.204
			Low RH	187	1,159.7	-3.3	0.886
			High RH	189	1,142.6	-20.4	0.385
			Low plus High RH	376	1,151.1	-11.9	0.498
19-13	IgM (mg/dL)[a]	0.020	Comparison	1,064	86.34		
			Background RH	315	85.85	-0.49	0.887
			Low RH	187	83.40	-2.94	0.477
			High RH	189	82.77	-3.57	0.396
			Low plus High RH	376	83.08	-3.26	0.300
20-8	FVC (percent of predicted)	0.147	Comparison	1,159	95.74		
			Background RH	348	96.17	0.44 (-1.45,2.32)	0.651
			Low RH	207	93.22	-2.52 (-4.81,-0.23)	0.031
			High RH	212	94.78	-0.96 (-3.30,1.38)	0.420
			Low plus High RH	419	94.01	-1.73 (-3.48,0.02)	0.052
20-10	FEV$_1$ (percent of predicted)	0.145	Comparison	1,159	85.33		
			Background RH	348	85.09	-0.23 (-2.22,1.76)	0.818
			Low RH	207	83.04	-2.29 (-4.71,0.13)	0.064
			High RH	212	85.19	-0.14 (-2.60,2.33)	0.915
			Low plus High RH	419	84.13	-1.20 (-3.04,0.65)	0.203
20-12	Ratio of Observed FEV$_1$ to Observed FVC[d]	0.214	Comparison	1,159	0.727		
			Background RH	348	0.723	-0.004	0.325
			Low RH	207	0.725	-0.002	0.683
			High RH	212	0.734	0.007	0.220
			Low plus High RH	419	0.730	0.003	0.572

[a]Means transformed from natural logarithm scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm scale; p-value based on difference of means on natural logarithm scale.

[b]Means transformed from square root scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on square root scale; p-value based on difference of means on square root scale.

[c]Means transformed from natural logarithm (clinical parameter + 0.1) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (clinical parameter + 0.1) scale; p-value based on difference of means on natural logarithm (clinical parameter + 0.1) scale.

[d]Means transformed from natural logarithm (1 – clinical parameter) scale; difference of means after transformation to original scale; confidence interval not given because analysis was performed on natural logarithm (1 – clinical parameter) scale; p-value based on difference of means on natural logarithm (1 – clinical parameter) scale.

Note: RH = Ranch Hand.
    Background: (Ranch Hand): 1987 dioxin ≤ 10 ppt.
    Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
    High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table G-16. Summary of Adjusted Results for Continuous Variables – Model 4 (Ranch Hands: Log$_2$ (1987 Dioxin))

Table Ref.	Clinical Parameter (Units)	R^2	Adjusted Slope (Standard Error)	p-Value
9-6	Body Mass Index (kg/m^2)[a]	0.112	0.026 (0.004)	<0.001
10-37	PSA (ng/mL)[a]	0.069	-0.008 (0.021)	0.713
12-20	WMS-R: Verbal Paired Associates	0.073	-0.060 (0.081)	0.458
12-21	WMS-R: Logical Memory, Immediate Recall	0.093	-0.050 (0.082)	0.541
12-22	WMS-R: Logical Memory, Delayed Recall	0.103	-0.028 (0.091)	0.762
12-23	WMS-R: Visual Reproduction, Immediate Recall	0.157	-0.054 (0.116)	0.643
12-24	WMS-R: Visual Reproduction, Delayed Recall	0.175	-0.090 (0.148)	0.541
13-11	AST (U/L)[a]	0.055	0.004 (0.009)	0.645
13-13	ALT (U/L)[a]	0.133	0.006 (0.007)	0.418
13-15	GGT (U/L)[a]	0.115	0.005 (0.013)	0.668
13-17	Alkaline Phosphatase (U/L)[a]	0.047	-0.011 (0.007)	0.131
13-19	Total Bilirubin (mg/dL)[a]	0.048	-0.011 (0.013)	0.384
13-22	LDH (U/L)[a]	0.026	-0.002 (0.005)	0.685
13-24	Cholesterol (mg/dL)[b]	0.076	-0.014 (0.033)	0.672
13-26	HDL Cholesterol (mg/dL)[a]	0.206	-0.003 (0.007)	0.693
13-28	Cholesterol-HDL Ratio[a]	0.145	0.000 (0.007)	0.956
13-30	Triglycerides (mg/dL)[a]	0.101	0.025 (0.014)	0.077
13-32	Creatine Phosphokinase (U/L)[a]	0.122	0.007 (0.015)	0.654
13-34	Serum Amylase (U/L)[a]	0.071	-0.020 (0.010)	0.048
13-40	Prealbumin (mg/dL)[b]	0.084	-0.002 (0.015)	0.886
13-42	Albumin (mg/dL)	0.054	-5.001 (7.248)	0.490
13-44	α-1-Acid Glycoprotein (mg/dL)[a]	0.080	-0.012 (0.006)	0.054
13-46	α-1-Antitrypsin (mg/dL)[b]	0.116	-0.001 (0.027)	0.982
13-48	α-2-Macroglobulin (mg/dL)[a]	0.176	-0.006 (0.007)	0.391
13-50	Apolipoprotein B (mg/dL)[b]	0.039	-0.007 (0.031)	0.830
13-52	C3 Complement (mg/dL)[b]	0.204	0.019 (0.023)	0.407
13-54	C4 Complement (mg/dL)[b]	0.075	-0.014 (0.015)	0.342
13-56	Haptoglobin (mg/dL)[b]	0.092	-0.065 (0.070)	0.348
13-58	Transferrin (mg/dL)[a]	0.043	0.008 (0.004)	0.057
13-60	Prothrombin Time (seconds)[a]	0.036	-0.003 (0.001)	0.050
14-11	Duration of Post-SEA Acne (months) (Excluding Participants with Pre-SEA Acne)[b]	0.206	0.964 (0.294)	0.002
14-12	Duration of Post-SEA Acne (months) (All Post-SEA Occurrences)[b]	0.026	0.206 (0.288)	0.475
15-7	Systolic Blood Pressure (mm Hg)[a]	0.070	-0.003 (0.004)	0.393
15-9	Diastolic Blood Pressure (mm Hg)[b]	0.141	-0.012 (0.014)	0.406
15-29	Resting Pressure Index	0.136	0.000 (0.004)	0.991
15-31	Hyperemic Pressure Index (1 Minute Post-exercise)	0.176	-0.001 (0.005)	0.888
15-33	Hyperemic Pressure Index (2 Minutes Post-exercise)	0.184	-0.002 (0.004)	0.579
16-3	RBC Count (million/mm^3)	0.085	-0.020 (0.012)	0.099
16-5	WBC Count (thousand/mm^3)[a]	0.151	-0.014 (0.007)	0.047
16-7	Hemoglobin (gm/dL)	0.082	-0.020 (0.032)	0.519
16-9	Hematocrit (percent)	0.067	-0.108 (0.102)	0.290
16-11	Platelet Count (thousand/mm^3)[b]	0.087	0.004 (0.048)	0.932
16-14	Absolute Neutrophils (Segs) (thousand/mm^3)[b]	0.120	-0.008 (0.008)	0.364

Table Ref.	Clinical Parameter (Units)	R^2	Adjusted Slope (Standard Error)	p-Value
16-15	Absolute Neutrophils (Bands) (thousand/mm^3) (Nonzero Measurements)[a]	0.037	0.012 (0.025)	0.613
16-17	Absolute Lymphocytes (thousand/mm^3)[a]	0.056	-0.007 (0.011)	0.521
16-18	Absolute Monocytes (thousand/mm^3)[b]	0.041	-0.003 (0.004)	0.457
16-19	Absolute Eosinophils (thousand/mm^3) (Nonzero Measurements)[a]	0.039	-0.031 (0.020)	0.121
16-21	Absolute Basophils (thousand/mm^3) (Nonzero Measurements)[a]	0.046	0.020 (0.017)	0.235
16-23	Fibrinogen (mg/dL)[a]	0.124	0.004 (0.005)	0.411
16-25	Erythrocyte Sedimentation Rate (mm/hr)[c]	0.095	0.042 (0.024)	0.086
17-5	Blood Urea Nitrogen (mg/dL)[a]	0.071	0.004 (0.007)	0.596
17-6	Serum Creatinine (mg/dL)[a]	0.059	-0.002 (0.004)	0.590
17-7	Creatinine Clearance[b]	0.343	0.118 (0.025)	<0.001
17-8	Urinary Microalbumin to Urinary Creatinine Ratio (μg/mg) (Nonzero Measurements)[a]	0.266	0.057 (0.096)	0.553
17-10	Urine Specific Gravity	0.047	0.0000 (0.0002)	0.807
18-12	TSH (μIU/mL)[a]	0.064	-0.003 (0.014)	0.854
18-14	Free T$_4$ (ng/dL)[a]	0.030	0.001 (0.004)	0.775
18-17	Fasting Glucose (mg/dL)[a]	0.095	0.010 (0.005)	0.068
18-19	2-hour Postprandial Glucose (mg/dL) (Nondiabetics Only)[a]	0.126	-0.007 (0.010)	0.492
18-22	Fasting Insulin (μIU/mL)[a]	0.307	0.013 (0.014)	0.349
18-24	2-hour Postprandial Insulin (μIU/mL) (Nondiabetics Only)[a]	0.222	-0.002 (0.022)	0.937
18-26	Hemoglobin A1c (percent) (Diabetics Only)[a]	0.115	0.019 (0.011)	0.095
18-28	C-peptide (ng/mL) (Diabetics Only)[b]	0.252	-0.014 (0.027)	0.598
18-30	Proinsulin (pmol/L) (Diabetics Only)[a]	0.196	-0.001 (0.071)	0.993
18-33	Total Testosterone (ng/dL)[b]	0.176	0.009 (0.115)	0.939
18-35	Free Testosterone (pg/mL)[b]	0.179	-0.011 (0.014)	0.460
18-37	Estradiol (pg/mL) (Measurements Above Sensitivity Limit)[a]	0.009	0.006 (0.017)	0.708
18-39	LH (mIU/mL)[a]	0.049	-0.016 (0.016)	0.321
18-41	FSH (mIU/mL)[a]	0.076	0.011 (0.017)	0.523
19-4	CD3+ Cells (T Cells) (cells/mm^3)[a]	0.081	0.016 (0.020)	0.419
19-5	CD4+ Cells (Helper T Cells) (cells/mm^3)[b]	0.089	0.288 (0.272)	0.292
19-6	CD8+ Cells (Suppressor Cells) (cells/mm^3)[a]	0.055	0.007 (0.024)	0.769
19-7	CD16+56+ Cells (Natural Killer Cells) (cells/mm^3)[a]	0.059	-0.009 (0.026)	0.726
19-8	CD20+ Cells (B Cells) (cells/mm^3)[a]	0.128	0.014 (0.028)	0.601
19-9	CD3+CD4+ Cells (Helper Cells) (cells/mm^3)[b]	0.092	0.248 (0.272)	0.362
19-10	Absolute Lymphocytes (cells/mm^3)[a]	0.074	-0.004 (0.011)	0.704
19-11	IgA (mg/dL)[b]	0.034	0.098 (0.105)	0.354
19-12	IgG (mg/dL)[a]	0.063	-0.001 (0.007)	0.885
19-13	IgM (mg/dL)[a]	0.036	-0.023 (0.017)	0.188
20-8	FVC (percent of predicted)	0.166	-0.631 (0.393)	0.109
20-10	FEV$_1$ (percent of predicted)	0.170	-0.169 (0.421)	0.688
20-12	Ratio of Observed FEV$_1$ to Observed FVC[d]	0.238	-0.012 (0.007)	0.083

[a]Slope and standard error based on natural logarithm of clinical parameter versus log₂ (1987 dioxin).
[b]Slope and standard error based on square root of clinical parameter versus log₂ (1987 dioxin).
[c]Slope and standard error based on natural logarithm of (clinical parameter + 0.1) versus log₂ (1987 dioxin).
[d]Slope and standard error based on natural logarithm of (1 – clinical parameter) versus log₂ (1987 dioxin).

Table G-17. Summary of Adjusted Results for Dichotomous Variables – Model 1 (Ranch Hands vs. Comparisons)

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
9-3	Self-perception of Health	All	1.03 (0.79,1.36)	0.822
		Officer	1.24 (0.74,2.10)	0.416
		Enlisted Flyer	0.78 (0.42,1.42)	0.413
		Enlisted Groundcrew	1.05 (0.72,1.53)	0.805
9-4	Appearance of Illness or Distress	All	0.94 (0.58,1.50)	0.789
		Officer	1.03 (0.48,2.19)	0.946
		Enlisted Flyer	1.90 (0.72,4.98)	0.193
		Enlisted Groundcrew	0.52 (0.23,1.21)	0.129
9-5	Relative Age Appearance	All	1.28 (0.82,1.98)	0.277
		Officer	1.33 (0.44,3.99)	0.616
		Enlisted Flyer	1.05 (0.48,2.29)	0.906
		Enlisted Groundcrew	1.42 (0.78,2.58)	0.255
9-7	Body Mass Index	All	1.02 (0.84,1.24)	0.827
		Officer	1.03 (0.75,1.41)	0.873
		Enlisted Flyer	1.01 (0.63,1.62)	0.976
		Enlisted Groundcrew	1.02 (0.77,1.36)	0.874
10-3	All Skin Neoplasms	All	1.28 (1.06,1.56)	0.012
		Officer	1.32 (0.98,1.79)	0.069
		Enlisted Flyer	1.23 (0.76,1.98)	0.400
		Enlisted Groundcrew	1.26 (0.94,1.70)	0.122
10-4	Malignant Skin Neoplasms	All	1.23 (0.97,1.55)	0.089
		Officer	1.33 (0.95,1.87)	0.100
		Enlisted Flyer	1.40 (0.80,2.44)	0.235
		Enlisted Groundcrew	1.03 (0.69,1.53)	0.889
10-5	Benign Skin Neoplasms	All	1.19 (0.98,1.44)	0.079
		Officer	1.21 (0.89,1.65)	0.213
		Enlisted Flyer	1.10 (0.69,1.76)	0.697
		Enlisted Groundcrew	1.20 (0.90,1.61)	0.214
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	All	2.55 (0.82,7.97)	0.100
		Officer	2.68 (0.63,11.50)	0.184
		Enlisted Flyer	--	--
		Enlisted Groundcrew	2.41 (0.39,14.92)	0.344
10-7	Basal Cell Carcinoma	All	1.33 (1.03,1.71)	0.027
		Officer	1.58 (1.10,2.27)	0.013
		Enlisted Flyer	1.39 (0.76,2.51)	0.284
		Enlisted Groundcrew	1.02 (0.66,1.57)	0.936
10-8	Squamous Cell Carcinoma	All	1.08 (0.71,1.63)	0.728
		Officer	0.97 (0.55,1.70)	0.916
		Enlisted Flyer	1.53 (0.55,4.24)	0.417
		Enlisted Groundcrew	1.08 (0.50,2.34)	0.847

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
10-9	Nonmelanoma	All	1.31 (1.03,1.67)	0.027
		Officer	1.46 (1.03,2.07)	0.032
		Enlisted Flyer	1.58 (0.90,2.78)	0.110
		Enlisted Groundcrew	1.02 (0.68,1.55)	0.907
10-10	Melanoma	All	0.93 (0.52,1.68)	0.813
		Officer	1.03 (0.47,2.27)	0.937
		Enlisted Flyer	0.25 (0.03,2.19)	0.210
		Enlisted Groundcrew	1.18 (0.43,3.23)	0.755
10-11	Systemic Neoplasms	All	1.01 (0.80,1.28)	0.939
		Officer	1.00 (0.72,1.39)	0.996
		Enlisted Flyer	1.12 (0.68,1.84)	0.656
		Enlisted Groundcrew	0.98 (0.70,1.37)	0.892
10-12	Malignant Systemic Neoplasms	All	1.37 (0.96,1.96)	0.082
		Officer	1.81 (1.13,2.91)	0.014
		Enlisted Flyer	1.87 (0.94,3.71)	0.073
		Enlisted Groundcrew	0.72 (0.40,1.30)	0.281
10-13	Benign Systemic Neoplasms	All	0.96 (0.74,1.23)	0.731
		Officer	0.85 (0.60,1.21)	0.368
		Enlisted Flyer	0.84 (0.48,1.46)	0.528
		Enlisted Groundcrew	1.14 (0.80,1.63)	0.474
10-14	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	All	0.71 (0.34,1.49)	0.368
		Officer	0.66 (0.24,1.77)	0.407
		Enlisted Flyer	1.61 (0.25,10.19)	0.613
		Enlisted Groundcrew	0.59 (0.19,1.87)	0.372
10-16	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	All	0.30 (0.03,3.47)	0.316
		Officer	--	--
		Enlisted Flyer	1.08 (0.05,21.84)	0.959
		Enlisted Groundcrew	--	--
10-17	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	All	0.81 (0.20,3.25)	0.761
		Officer	0.76 (0.07,8.20)	0.823
		Enlisted Flyer	2.69 (0.35,20.72)	0.341
		Enlisted Groundcrew	--	--
10-18	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	All	7.34 (0.19,289.00)	0.247
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
10-19	Malignant Systemic Neoplasms (Thyroid Gland)	All	0.70 (0.05,10.41)	0.794
		Officer	1.58 (0.08,33.16)	0.768
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
10-20	Malignant Systemic Neoplasms (Bronchus and Lung)	All	2.27 (0.78,6.62)	0.120
		Officer	2.63 (0.59,11.86)	0.207
		Enlisted Flyer	1.14 (0.20,6.64)	0.882
		Enlisted Groundcrew	4.39 (0.45,43.11)	0.205

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
10-21	All Stomach Neoplasms	All	0.73 (0.22,2.43)	0.609
		Officer	0.22 (0.02,1.99)	0.176
		Enlisted Flyer	2.58 (0.24,27.52)	0.433
		Enlisted Groundcrew	1.02 (0.13,7.98)	0.983
10-22	Malignant Systemic Neoplasms (Colon and Rectum)	All	2.03 (0.68,6.00)	0.188
		Officer	4.66 (1.04,20.80)	0.044
		Enlisted Flyer	0.53 (0.05,5.77)	0.600
		Enlisted Groundcrew	1.20 (0.23,6.38)	0.828
10-23	Malignant Systemic Neoplasms (Urinary System)	All	3.02 (1.16,7.89)	0.018
		Officer	3.59 (1.01,12.81)	0.049
		Enlisted Flyer	7.36 (0.73,73.97)	0.090
		Enlisted Groundcrew	1.77 (0.45,6.91)	0.413
10-24	Malignant Systemic Neoplasms (Kidney and Ureter)	All	2.87 (0.57,14.50)	0.181
		Officer	4.21 (0.31,56.80)	0.279
		Enlisted Flyer	--	--
		Enlisted Groundcrew	1.87 (0.27,12.70)	0.523
10-25	Malignant Systemic Neoplasms (Prostate)	All	1.28 (0.80,2.05)	0.303
		Officer	1.42 (0.77,2.62)	0.257
		Enlisted Flyer	2.13 (0.85,5.35)	0.106
		Enlisted Groundcrew	0.77 (0.33,1.67)	0.512
10-26	Malignant Systemic Neoplasms (Penis and Other Male Genital Organs)	All	--	--
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
10-27	Malignant Systemic Neoplasms (Testicles)	All	--	--
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
10-28	Malignant Systemic Neoplasms (Bone and Articular Cartilage)	All	--	--
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	All	0.20 (0.02,1.84)	0.109
		Officer	--	--
		Enlisted Flyer	1.28 (0.07,23.07)	0.866
		Enlisted Groundcrew	--	--
10-30	Carcinoma in Situ	All	4.71 (0.56,39.47)	0.137
		Officer	17.42 (0.82,372.10)	0.067
		Enlisted Flyer	6.86 (0.35,134.80)	0.205
		Enlisted Groundcrew	--	--
10-31	Hodgkin's Disease	All	1.47 (0.09,24.30)	0.786
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
10-32	Leukemia	All	1.17 (0.23,5.93)	0.845
		Officer	1.31 (0.22,7.93)	0.770
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
10-33	Other Malignant Systemic Neoplasms (Lymphoid and Histiocytic Tissue)	All	0.74 (0.23,2.36)	0.606
		Officer	2.00 (0.31,12.97)	0.467
		Enlisted Flyer	0.22 (0.02,2.21)	0.199
		Enlisted Groundcrew	0.71 (0.11,4.63)	0.719
10-34	Lymphoreticular Sarcoma	All	0.67 (0.05,9.60)	0.765
		Officer	0.77 (0.05,10.98)	0.847
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
10-35	Skin and Systemic Neoplasms	All	1.09 (0.86,1.38)	0.491
		Officer	1.12 (0.79,1.59)	0.517
		Enlisted Flyer	1.10 (0.65,1.85)	0.725
		Enlisted Groundcrew	1.06 (0.77,1.46)	0.734
10-36	Malignant Skin and Systemic Neoplasms	All	1.14 (0.88,1.47)	0.329
		Officer	1.28 (0.91,1.82)	0.161
		Enlisted Flyer	1.47 (0.87,2.49)	0.152
		Enlisted Groundcrew	0.86 (0.59,1.27)	0.450
10-38	PSA	All	1.07 (0.62,1.86)	0.800
		Officer	1.19 (0.60,2.35)	0.621
		Enlisted Flyer	0.98 (0.30,3.16)	0.967
		Enlisted Groundcrew	0.94 (0.39,2.27)	0.887
11-3	Inflammatory Diseases	All	2.43 (0.87,6.74)	0.088
		Officer	5.34 (0.55,52.27)	0.150
		Enlisted Flyer	2.91 (0.25,33.21)	0.390
		Enlisted Groundcrew	1.67 (0.43,6.45)	0.460
11-4	Hereditary and Degenerative Diseases	All	1.20 (0.92,1.56)	0.173
		Officer	1.57 (1.04,2.36)	0.030
		Enlisted Flyer	1.40 (0.77,2.56)	0.266
		Enlisted Groundcrew	0.85 (0.57,1.29)	0.455
11-5	Peripheral Disorders	All	1.03 (0.83,1.28)	0.795
		Officer	1.19 (0.85,1.68)	0.310
		Enlisted Flyer	0.92 (0.55,1.55)	0.758
		Enlisted Groundcrew	0.93 (0.67,1.31)	0.696
11-6	Other Neurological Disorders	All	1.16 (0.90,1.50)	0.239
		Officer	0.84 (0.49,1.44)	0.531
		Enlisted Flyer	1.43 (0.85,2.40)	0.181
		Enlisted Groundcrew	1.22 (0.87,1.72)	0.251
11-7	Smell	All	1.21 (0.67,2.18)	0.531
		Officer	0.90 (0.37,2.23)	0.827
		Enlisted Flyer	0.82 (0.19,3.56)	0.792
		Enlisted Groundcrew	1.94 (0.77,4.87)	0.161

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
11-8	Visual Fields	All	3.08 (1.13,8.41)	0.022
		Officer	4.88 (0.97,24.68)	0.055
		Enlisted Flyer	--	--
		Enlisted Groundcrew	1.20 (0.26,5.50)	0.814
11-9	Light Reaction	All	0.72 (0.21,2.44)	0.594
		Officer	0.76 (0.07,8.57)	0.828
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.75 (0.18,3.14)	0.699
11-10	Ocular Movement	All	2.21 (0.57,8.52)	0.248
		Officer	1.74 (0.24,12.70)	0.587
		Enlisted Flyer	--	--
		Enlisted Groundcrew	1.92 (0.26,14.08)	0.519
11-11	Facial Sensation	All	2.74 (0.48,15.76)	0.244
		Officer	1.31 (0.08,21.52)	0.850
		Enlisted Flyer	1.06 (0.06,19.00)	0.969
		Enlisted Groundcrew	--	--
11-12	Corneal Reflex	All	0.55 (0.10,3.00)	0.479
		Officer	0.78 (0.07,9.04)	0.845
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.69 (0.06,8.16)	0.771
11-13	Smile	All	1.07 (0.40,2.88)	0.895
		Officer	0.78 (0.21,2.92)	0.708
		Enlisted Flyer	1.01 (0.06,16.77)	0.994
		Enlisted Groundcrew	1.99 (0.33,12.14)	0.457
11-14	Palpebral Fissure	All	1.57 (0.86,2.87)	0.143
		Officer	1.36 (0.54,3.41)	0.514
		Enlisted Flyer	1.31 (0.37,4.67)	0.680
		Enlisted Groundcrew	2.09 (0.76,5.73)	0.151
11-15	Balance	All	1.13 (0.59,2.18)	0.717
		Officer	1.64 (0.64,4.25)	0.304
		Enlisted Flyer	1.15 (0.31,4.19)	0.837
		Enlisted Groundcrew	0.56 (0.14,2.18)	0.400
11-16	Gag Reflex	All	3.09 (0.24,39.24)	0.367
		Officer	--	--
		Enlisted Flyer	1.45 (0.04,56.04)	0.842
		Enlisted Groundcrew	--	--
11-17	Speech	All	1.73 (0.69,4.30)	0.244
		Officer	1.69 (0.41,6.93)	0.469
		Enlisted Flyer	--	--
		Enlisted Groundcrew	1.47 (0.42,5.11)	0.545
11-18	Tongue Position Relative to Midline	All	2.22 (0.35,14.03)	0.390
		Officer	1.57 (0.09,26.03)	0.753
		Enlisted Flyer	1.17 (0.07,19.65)	0.916
		Enlisted Groundcrew	--	--

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
11-19	Shoulder Shrug	All	0.92 (0.22,3.90)	0.909
		Officer	1.61 (0.22,11.81)	0.638
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.80 (0.07,9.06)	0.860
11-20	Cranial Nerve Index	All	1.47 (1.06,2.04)	0.020
		Officer	1.54 (0.93,2.53)	0.091
		Enlisted Flyer	1.31 (0.61,2.82)	0.487
		Enlisted Groundcrew	1.49 (0.89,2.47)	0.128
11-21	Pinprick	All	1.24 (0.86,1.77)	0.245
		Officer	1.16 (0.66,2.06)	0.606
		Enlisted Flyer	1.04 (0.47,2.29)	0.920
		Enlisted Groundcrew	1.42 (0.82,2.46)	0.206
11-22	Light Touch	All	1.08 (0.69,1.69)	0.741
		Officer	1.34 (0.64,2.80)	0.430
		Enlisted Flyer	0.68 (0.25,1.87)	0.460
		Enlisted Groundcrew	1.11 (0.56,2.17)	0.768
11-23	Muscle Status	All	1.07 (0.70,1.63)	0.746
		Officer	1.12 (0.58,2.19)	0.737
		Enlisted Flyer	0.87 (0.34,2.28)	0.784
		Enlisted Groundcrew	1.13 (0.59,2.14)	0.716
11-27	Babinski Reflex	All	0.82 (0.37,1.83)	0.634
		Officer	1.16 (0.25,5.29)	0.851
		Enlisted Flyer	1.32 (0.32,5.52)	0.700
		Enlisted Groundcrew	0.47 (0.13,1.75)	0.260
11-28	Any Symmetric Peripheral Abnormality	All	1.14 (0.90,1.45)	0.288
		Officer	1.19 (0.82,1.73)	0.357
		Enlisted Flyer	1.18 (0.68,2.05)	0.560
		Enlisted Groundcrew	1.07 (0.73,1.57)	0.716
11-29	Possible Peripheral Neuropathy	All	1.10 (0.86,1.41)	0.443
		Officer	1.11 (0.76,1.63)	0.585
		Enlisted Flyer	1.16 (0.66,2.04)	0.602
		Enlisted Groundcrew	1.06 (0.72,1.57)	0.754
11-30	Probable Peripheral Neuropathy	All	1.19 (0.81,1.75)	0.380
		Officer	1.47 (0.84,2.57)	0.179
		Enlisted Flyer	1.33 (0.56,3.14)	0.522
		Enlisted Groundcrew	0.84 (0.43,1.63)	0.597
11-31	Tremor	All	0.93 (0.65,1.34)	0.705
		Officer	0.89 (0.50,1.60)	0.700
		Enlisted Flyer	0.97 (0.41,2.28)	0.950
		Enlisted Groundcrew	0.95 (0.56,1.63)	0.861
11-32	Coordination	All	0.75 (0.47,1.19)	0.218
		Officer	0.99 (0.47,2.07)	0.971
		Enlisted Flyer	0.63 (0.22,1.76)	0.373
		Enlisted Groundcrew	0.64 (0.31,1.31)	0.223

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
11-33	Romberg Sign	All	1.13 (0.59,2.18)	0.717
		Officer	1.64 (0.64,4.25)	0.304
		Enlisted Flyer	1.15 (0.31,4.19)	0.837
		Enlisted Groundcrew	0.56 (0.14,2.18)	0.400
11-34	Gait	All	0.97 (0.68,1.37)	0.861
		Officer	1.11 (0.64,1.90)	0.716
		Enlisted Flyer	0.81 (0.37,1.76)	0.590
		Enlisted Groundcrew	0.93 (0.54,1.61)	0.788
11-35	CNS Index	All	0.88 (0.68,1.15)	0.359
		Officer	1.01 (0.66,1.55)	0.948
		Enlisted Flyer	0.80 (0.43,1.48)	0.480
		Enlisted Groundcrew	0.81 (0.54,1.22)	0.315
12-3	Psychoses	All	0.97 (0.65,1.44)	0.876
		Officer	0.77 (0.32,1.85)	0.562
		Enlisted Flyer	1.73 (0.74,4.06)	0.208
		Enlisted Groundcrew	0.85 (0.50,1.43)	0.538
12-4	Alcohol Dependence	All	1.06 (0.71,1.59)	0.774
		Officer	0.68 (0.30,1.52)	0.350
		Enlisted Flyer	0.84 (0.33,2.14)	0.716
		Enlisted Groundcrew	1.43 (0.83,2.47)	0.196
12-5	Drug Dependence	All	0.67 (0.12,3.77)	0.647
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.89 (0.15,5.40)	0.899
12-6	Anxiety	All	1.06 (0.86,1.30)	0.598
		Officer	0.83 (0.56,1.22)	0.336
		Enlisted Flyer	1.09 (0.67,1.78)	0.735
		Enlisted Groundcrew	1.21 (0.90,1.62)	0.201
12-7	Other Neuroses	All	1.01 (0.83,1.23)	0.901
		Officer	0.73 (0.54,0.99)	0.043
		Enlisted Flyer	1.19 (0.72,1.97)	0.491
		Enlisted Groundcrew	1.34 (0.98,1.82)	0.067
12-8	SCL-90-R Anxiety	All	0.88 (0.63,1.24)	0.459
		Officer	0.58 (0.25,1.33)	0.196
		Enlisted Flyer	0.83 (0.38,1.81)	0.640
		Enlisted Groundcrew	1.01 (0.66,1.55)	0.964
12-9	SCL-90-R Depression	All	0.85 (0.63,1.15)	0.285
		Officer	0.74 (0.41,1.31)	0.298
		Enlisted Flyer	0.76 (0.36,1.60)	0.469
		Enlisted Groundcrew	0.94 (0.63,1.40)	0.764
12-10	SCL-90-R Hostility	All	0.96 (0.63,1.45)	0.839
		Officer	0.48 (0.15,1.51)	0.210
		Enlisted Flyer	0.66 (0.27,1.64)	0.370
		Enlisted Groundcrew	1.29 (0.76,2.18)	0.339

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
12-11	SCL-90-R Interpersonal Sensitivity	All	0.65 (0.46,0.92)	0.013
		Officer	0.47 (0.23,0.98)	0.045
		Enlisted Flyer	0.66 (0.31,1.41)	0.287
		Enlisted Groundcrew	0.74 (0.47,1.16)	0.195
12-12	SCL-90-R Obsessive-compulsive Behavior	All	0.88 (0.68,1.13)	0.310
		Officer	0.85 (0.53,1.36)	0.492
		Enlisted Flyer	0.89 (0.49,1.62)	0.713
		Enlisted Groundcrew	0.89 (0.62,1.26)	0.505
12-13	SCL-90-R Paranoid Ideation	All	0.53 (0.32,0.88)	0.011
		Officer	0.39 (0.11,1.42)	0.153
		Enlisted Flyer	0.85 (0.26,2.80)	0.793
		Enlisted Groundcrew	0.51 (0.27,0.95)	0.033
12-14	SCL-90-R Phobic Anxiety	All	0.82 (0.57,1.17)	0.275
		Officer	0.42 (0.15,1.15)	0.090
		Enlisted Flyer	0.87 (0.40,1.85)	0.709
		Enlisted Groundcrew	0.94 (0.60,1.48)	0.795
12-15	SCL-90-R Psychoticism	All	0.87 (0.63,1.20)	0.397
		Officer	0.92 (0.50,1.69)	0.784
		Enlisted Flyer	0.78 (0.36,1.69)	0.528
		Enlisted Groundcrew	0.88 (0.57,1.36)	0.558
12-16	SCL-90-R Somatization	All	0.90 (0.68,1.19)	0.452
		Officer	0.93 (0.52,1.64)	0.799
		Enlisted Flyer	1.14 (0.63,2.05)	0.670
		Enlisted Groundcrew	0.81 (0.56,1.18)	0.267
12-17	SCL-90-R Global Severity Index	All	0.81 (0.59,1.10)	0.166
		Officer	0.69 (0.36,1.33)	0.268
		Enlisted Flyer	0.67 (0.31,1.42)	0.297
		Enlisted Groundcrew	0.90 (0.61,1.33)	0.592
12-18	SCL-90-R Positive Symptom Total	All	0.72 (0.53,0.98)	0.033
		Officer	0.61 (0.33,1.13)	0.117
		Enlisted Flyer	0.69 (0.31,1.50)	0.345
		Enlisted Groundcrew	0.78 (0.52,1.17)	0.227
12-19	SCL-90-R Positive Symptom Distress Index	All	0.84 (0.59,1.20)	0.340
		Officer	0.99 (0.41,2.35)	0.976
		Enlisted Flyer	0.43 (0.20,0.95)	0.036
		Enlisted Groundcrew	1.04 (0.65,1.64)	0.877
13-3	Uncharacterized Hepatitis	All	1.53 (0.74,3.15)	0.255
		Officer	0.75 (0.19,3.04)	0.688
		Enlisted Flyer	3.72 (0.38,36.41)	0.259
		Enlisted Groundcrew	1.82 (0.69,4.80)	0.224
13-4	Jaundice	All	0.64 (0.34,1.20)	0.153
		Officer	0.66 (0.27,1.63)	0.368
		Enlisted Flyer	2.50 (0.22,28.01)	0.457
		Enlisted Groundcrew	0.48 (0.17,1.32)	0.155

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	All	1.10 (0.68,1.79)	0.690
		Officer	1.59 (0.68,3.71)	0.281
		Enlisted Flyer	1.25 (0.36,4.34)	0.720
		Enlisted Groundcrew	0.84 (0.43,1.67)	0.626
13-6	Chronic Liver Disease and Cirrhosis (Nonalcohol-related)	All	1.50 (0.87,2.60)	0.144
		Officer	2.07 (0.82,5.23)	0.124
		Enlisted Flyer	0.18 (0.02,1.50)	0.113
		Enlisted Groundcrew	1.98 (0.91,4.31)	0.086
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	All	3.97 (0.76,20.87)	0.082
		Officer	3.05 (0.27,33.85)	0.364
		Enlisted Flyer	--	--
		Enlisted Groundcrew	5.03 (0.50,50.97)	0.172
13-8	Enlarged Liver	All	0.92 (0.56,1.51)	0.746
		Officer	1.20 (0.54,2.70)	0.654
		Enlisted Flyer	1.17 (0.35,3.97)	0.798
		Enlisted Groundcrew	0.69 (0.33,1.44)	0.324
13-9	Other Disorders of the Liver	All	1.08 (0.89,1.30)	0.442
		Officer	1.01 (0.75,1.36)	0.941
		Enlisted Flyer	1.14 (0.72,1.80)	0.566
		Enlisted Groundcrew	1.11 (0.84,1.47)	0.461
13-10	Current Hepatomegaly	All	1.37 (0.62,3.02)	0.440
		Officer	2.25 (0.63,8.04)	0.214
		Enlisted Flyer	--	--
		Enlisted Groundcrew	1.83 (0.55,6.06)	0.323
13-12	AST	All	1.22 (0.87,1.72)	0.253
		Officer	1.53 (0.90,2.62)	0.120
		Enlisted Flyer	1.36 (0.55,3.33)	0.503
		Enlisted Groundcrew	0.96 (0.57,1.61)	0.884
13-14	ALT	All	0.93 (0.65,1.32)	0.670
		Officer	1.35 (0.73,2.47)	0.337
		Enlisted Flyer	0.84 (0.37,1.94)	0.687
		Enlisted Groundcrew	0.73 (0.43,1.24)	0.247
13-16	GGT	All	0.92 (0.67,1.25)	0.578
		Officer	1.09 (0.66,1.81)	0.727
		Enlisted Flyer	0.81 (0.38,1.70)	0.577
		Enlisted Groundcrew	0.83 (0.53,1.32)	0.432
13-18	Alkaline Phosphatase	All	1.37 (0.96,1.96)	0.086
		Officer	1.07 (0.53,2.16)	0.843
		Enlisted Flyer	1.13 (0.53,2.40)	0.752
		Enlisted Groundcrew	1.70 (1.03,2.80)	0.039
13-20	Total Bilirubin	All	1.02 (0.70,1.48)	0.921
		Officer	1.06 (0.60,1.87)	0.838
		Enlisted Flyer	1.62 (0.60,4.34)	0.342
		Enlisted Groundcrew	0.84 (0.47,1.50)	0.553

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
13-21	Direct Bilirubin	All	0.24 (0.05,1.14)	0.041
		Officer	0.48 (0.09,2.67)	0.401
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
13-23	LDH	All	1.25 (0.92,1.70)	0.159
		Officer	1.44 (0.90,2.31)	0.125
		Enlisted Flyer	1.58 (0.75,3.30)	0.228
		Enlisted Groundcrew	0.96 (0.59,1.58)	0.885
13-25	Cholesterol	All	0.78 (0.58,1.04)	0.088
		Officer	0.78 (0.46,1.33)	0.369
		Enlisted Flyer	0.96 (0.49,1.89)	0.908
		Enlisted Groundcrew	0.72 (0.48,1.08)	0.112
13-27	HDL Cholesterol	All	1.25 (0.97,1.62)	0.086
		Officer	1.52 (0.98,2.36)	0.064
		Enlisted Flyer	0.93 (0.50,1.73)	0.825
		Enlisted Groundcrew	1.22 (0.85,1.76)	0.289
13-29	Cholesterol-HDL Ratio	All	0.94 (0.76,1.15)	0.537
		Officer	0.88 (0.62,1.25)	0.481
		Enlisted Flyer	0.77 (0.47,1.26)	0.305
		Enlisted Groundcrew	1.05 (0.78,1.41)	0.745
13-31	Triglycerides	All	1.40 (1.05,1.88)	0.023
		Officer	1.22 (0.71,2.09)	0.474
		Enlisted Flyer	1.34 (0.66,2.70)	0.415
		Enlisted Groundcrew	1.54 (1.03,2.29)	0.034
13-33	Creatine Phosphokinase	All	0.82 (0.60,1.14)	0.242
		Officer	0.92 (0.54,1.59)	0.776
		Enlisted Flyer	0.70 (0.32,1.53)	0.375
		Enlisted Groundcrew	0.80 (0.50,1.29)	0.365
13-35	Serum Amylase	All	0.78 (0.45,1.36)	0.378
		Officer	0.27 (0.08,0.93)	0.038
		Enlisted Flyer	1.00 (0.29,3.41)	0.999
		Enlisted Groundcrew	1.25 (0.59,2.66)	0.566
13-36	Antibodies for Hepatitis A	All	0.86 (0.70,1.05)	0.136
		Officer	0.83 (0.59,1.16)	0.267
		Enlisted Flyer	1.04 (0.65,1.66)	0.871
		Enlisted Groundcrew	0.81 (0.60,1.10)	0.185
13-37	Serological Evidence of Prior Hepatitis B Infection	All	0.53 (0.38,0.76)	<0.001
		Officer	0.40 (0.17,0.93)	0.034
		Enlisted Flyer	0.59 (0.30,1.15)	0.123
		Enlisted Groundcrew	0.56 (0.35,0.90)	0.016
13-38	Antibodies for Hepatitis C	All	0.37 (0.13,1.02)	0.037
		Officer	0.74 (0.07,8.20)	0.805
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.45 (0.14,1.41)	0.170

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
13-39	Stool Hemoccult	All	1.27 (0.58,2.78)	0.545
		Officer	8.99 (1.07,75.33)	0.043
		Enlisted Flyer	2.00 (0.33,12.26)	0.454
		Enlisted Groundcrew	0.42 (0.12,1.51)	0.184
13-41	Prealbumin	All	1.61 (0.78,3.32)	0.198
		Officer	1.77 (0.59,5.36)	0.309
		Enlisted Flyer	0.39 (0.04,3.82)	0.415
		Enlisted Groundcrew	2.16 (0.72,6.54)	0.171
13-43	Albumin	All	1.23 (0.36,4.20)	0.736
		Officer	2.26 (0.36,14.04)	0.381
		Enlisted Flyer	1.75 (0.09,34.58)	0.712
		Enlisted Groundcrew	0.44 (0.04,4.55)	0.495
13-45	α-1-Acid Glycoprotein	All	1.23 (0.82,1.86)	0.323
		Officer	0.82 (0.38,1.73)	0.594
		Enlisted Flyer	2.20 (0.82,5.93)	0.118
		Enlisted Groundcrew	1.30 (0.73,2.32)	0.375
13-49	α-2-Macroglobulin	All	0.90 (0.68,1.19)	0.459
		Officer	1.16 (0.75,1.81)	0.506
		Enlisted Flyer	0.73 (0.39,1.37)	0.327
		Enlisted Groundcrew	0.78 (0.50,1.21)	0.263
13-51	Apolipoprotein B	All	0.52 (0.24,1.13)	0.084
		Officer	0.62 (0.19,2.00)	0.423
		Enlisted Flyer	0.27 (0.03,2.36)	0.237
		Enlisted Groundcrew	0.56 (0.18,1.79)	0.330
13-53	C3 Complement	All	0.68 (0.31,1.48)	0.321
		Officer	0.99 (0.39,2.47)	0.975
		Enlisted Flyer	0.23 (0.03,2.13)	0.198
		Enlisted Groundcrew	0.37 (0.04,3.42)	0.384
13-55	C4 Complement	All	0.93 (0.66,1.32)	0.688
		Officer	1.20 (0.71,2.01)	0.491
		Enlisted Flyer	0.75 (0.34,1.65)	0.475
		Enlisted Groundcrew	0.77 (0.43,1.38)	0.376
13-57	Haptoglobin	All	1.14 (0.86,1.51)	0.370
		Officer	1.18 (0.71,1.95)	0.526
		Enlisted Flyer	1.45 (0.78,2.68)	0.236
		Enlisted Groundcrew	1.00 (0.66,1.51)	0.998
13-59	Transferrin	All	0.87 (0.59,1.29)	0.494
		Officer	0.94 (0.53,1.67)	0.841
		Enlisted Flyer	0.48 (0.18,1.28)	0.141
		Enlisted Groundcrew	1.07 (0.55,2.09)	0.849
13-61	Prothrombin Time	All	0.85 (0.26,2.76)	0.792
		Officer	0.98 (0.16,6.16)	0.982
		Enlisted Flyer	0.77 (0.12,5.12)	0.786
		Enlisted Groundcrew	0.80 (0.07,9.25)	0.859

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
14-3	Acne (Lifetime)	All	1.34 (1.11,1.61)	0.002
		Officer	1.01 (0.75,1.36)	0.929
		Enlisted Flyer	1.58 (1.00,2.50)	0.051
		Enlisted Groundcrew	1.61 (1.22,2.14)	<0.001
14-4	Post-SEA Acne	All	1.43 (1.15,1.78)	0.001
		Officer	1.13 (0.76,1.67)	0.538
		Enlisted Flyer	1.59 (0.92,2.74)	0.096
		Enlisted Groundcrew	1.60 (1.18,2.16)	0.003
14-5	Post-SEA Acne (No Pre-SEA Acne)	All	1.78 (1.29,2.46)	<0.001
		Officer	1.11 (0.58,2.09)	0.759
		Enlisted Flyer	1.98 (0.88,4.43)	0.098
		Enlisted Groundcrew	2.15 (1.40,3.29)	<0.001
14-6	Post-SEA Acne (with Pre-SEA Acne)	All	1.11 (0.80,1.53)	0.532
		Officer	1.18 (0.70,2.00)	0.534
		Enlisted Flyer	1.16 (0.52,2.59)	0.713
		Enlisted Groundcrew	1.03 (0.64,1.67)	0.888
14-8	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (Excluding Participants with Pre-SEA Acne)	All	0.94 (0.49,1.82)	0.859
		Officer	0.50 (0.09,2.94)	0.444
		Enlisted Flyer	0.42 (0.08,2.13)	0.295
		Enlisted Groundcrew	1.34 (0.59,3.03)	0.481
14-10	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (All Post-SEA Occurrences)	All	1.07 (0.72,1.58)	0.752
		Officer	1.10 (0.51,2.36)	0.809
		Enlisted Flyer	0.70 (0.26,1.85)	0.470
		Enlisted Groundcrew	1.19 (0.70,2.01)	0.521
14-13	Acneiform Lesions	All	1.16 (0.77,1.73)	0.482
		Officer	1.44 (0.64,3.20)	0.376
		Enlisted Flyer	0.43 (0.14,1.37)	0.155
		Enlisted Groundcrew	1.34 (0.79,2.26)	0.274
14-14	Acneiform Scars	All	1.04 (0.72,1.52)	0.824
		Officer	1.51 (0.77,2.95)	0.230
		Enlisted Flyer	1.63 (0.71,3.71)	0.246
		Enlisted Groundcrew	0.67 (0.38,1.18)	0.166
14-15	Comedones	All	0.74 (0.50,1.10)	0.131
		Officer	0.46 (0.21,1.00)	0.049
		Enlisted Flyer	0.65 (0.30,1.40)	0.269
		Enlisted Groundcrew	1.10 (0.61,1.96)	0.755
14-16	Depigmentation	All	0.71 (0.39,1.27)	0.236
		Officer	0.89 (0.32,2.47)	0.823
		Enlisted Flyer	1.16 (0.35,3.90)	0.810
		Enlisted Groundcrew	0.47 (0.18,1.17)	0.105
14-17	Hyperpigmentation	All	0.84 (0.59,1.20)	0.334
		Officer	0.74 (0.41,1.36)	0.340
		Enlisted Flyer	0.79 (0.35,1.79)	0.566
		Enlisted Groundcrew	0.95 (0.57,1.57)	0.828

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
14-18	Inclusion Cysts	All	1.10 (0.83,1.46)	0.490
		Officer	0.71 (0.44,1.16)	0.171
		Enlisted Flyer	1.50 (0.80,2.83)	0.210
		Enlisted Groundcrew	1.35 (0.90,2.05)	0.151
14-19	Dermatology Index	All	0.98 (0.79,1.22)	0.855
		Officer	0.84 (0.57,1.21)	0.347
		Enlisted Flyer	1.14 (0.69,1.88)	0.609
		Enlisted Groundcrew	1.04 (0.76,1.42)	0.828
15-3	Essential Hypertension	All	0.92 (0.75,1.13)	0.418
		Officer	0.74 (0.53,1.02)	0.064
		Enlisted Flyer	0.96 (0.58,1.58)	0.870
		Enlisted Groundcrew	1.10 (0.81,1.50)	0.527
15-4	Heart Disease (Excluding Essential Hypertension)	All	1.20 (0.94,1.54)	0.146
		Officer	0.80 (0.53,1.21)	0.291
		Enlisted Flyer	2.46 (1.19,5.11)	0.015
		Enlisted Groundcrew	1.33 (0.94,1.89)	0.112
15-5	Myocardial Infarction	All	0.81 (0.59,1.12)	0.203
		Officer	0.77 (0.46,1.27)	0.307
		Enlisted Flyer	0.58 (0.28,1.20)	0.140
		Enlisted Groundcrew	1.01 (0.62,1.65)	0.956
15-6	Stroke or Transient Ischemic Attack	All	1.39 (0.82,2.34)	0.223
		Officer	1.30 (0.60,2.80)	0.507
		Enlisted Flyer	1.48 (0.45,4.81)	0.515
		Enlisted Groundcrew	1.46 (0.61,3.51)	0.401
15-8	Systolic Blood Pressure	All	0.87 (0.70,1.08)	0.203
		Officer	0.89 (0.63,1.24)	0.480
		Enlisted Flyer	0.76 (0.45,1.30)	0.323
		Enlisted Groundcrew	0.89 (0.63,1.26)	0.524
15-10	Diastolic Blood Pressure	All	1.17 (0.76,1.78)	0.473
		Officer	0.93 (0.43,2.01)	0.857
		Enlisted Flyer	1.00 (0.36,2.75)	0.998
		Enlisted Groundcrew	1.41 (0.78,2.54)	0.249
15-11	Heart Sounds	All	1.16 (0.79,1.69)	0.457
		Officer	0.91 (0.52,1.59)	0.732
		Enlisted Flyer	1.60 (0.60,4.27)	0.343
		Enlisted Groundcrew	1.37 (0.74,2.54)	0.316
15-12	Overall ECG	All	1.01 (0.82,1.24)	0.900
		Officer	0.93 (0.68,1.28)	0.670
		Enlisted Flyer	1.49 (0.92,2.41)	0.106
		Enlisted Groundcrew	0.93 (0.67,1.29)	0.653
15-13	ECG: RBBB	All	1.11 (0.68,1.80)	0.680
		Officer	1.54 (0.72,3.25)	0.263
		Enlisted Flyer	0.95 (0.37,2.40)	0.910
		Enlisted Groundcrew	0.82 (0.33,1.99)	0.656

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
15-14	ECG: LBBB	All	0.65 (0.27,1.59)	0.337
		Officer	0.14 (0.02,1.11)	0.062
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.86 (0.23,3.26)	0.826
15-15	ECG: Nonspecific ST- and T-wave Changes	All	1.02 (0.81,1.28)	0.860
		Officer	0.89 (0.62,1.27)	0.507
		Enlisted Flyer	1.48 (0.88,2.48)	0.141
		Enlisted Groundcrew	0.99 (0.69,1.42)	0.946
15-16	ECG: Bradycardia	All	1.43 (0.93,2.18)	0.104
		Officer	1.52 (0.85,2.73)	0.158
		Enlisted Flyer	2.78 (0.81,9.55)	0.103
		Enlisted Groundcrew	1.00 (0.47,2.10)	0.993
15-17	ECG: Tachycardia	All	0.67 (0.17,2.68)	0.562
		Officer	--	--
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.96 (0.22,4.19)	0.954
15-18	ECG: Arrhythmia	All	0.86 (0.63,1.19)	0.362
		Officer	0.96 (0.61,1.50)	0.854
		Enlisted Flyer	0.59 (0.26,1.31)	0.196
		Enlisted Groundcrew	0.89 (0.52,1.52)	0.668
15-19	ECG: Evidence of Prior Myocardial Infarction	All	0.80 (0.51,1.26)	0.331
		Officer	1.05 (0.55,1.98)	0.886
		Enlisted Flyer	0.54 (0.21,1.40)	0.201
		Enlisted Groundcrew	0.71 (0.31,1.63)	0.416
15-20	Funduscopic Examination	All	1.24 (0.89,1.73)	0.202
		Officer	1.06 (0.60,1.85)	0.851
		Enlisted Flyer	1.09 (0.52,2.29)	0.815
		Enlisted Groundcrew	1.49 (0.91,2.43)	0.111
15-21	Carotid Bruits	All	0.76 (0.40,1.48)	0.418
		Officer	0.48 (0.18,1.26)	0.136
		Enlisted Flyer	1.11 (0.21,5.81)	0.903
		Enlisted Groundcrew	1.33 (0.43,4.09)	0.624
15-22	Radial Pulses	All	0.91 (0.62,1.32)	0.602
		Officer	1.09 (0.62,1.93)	0.760
		Enlisted Flyer	0.47 (0.15,1.50)	0.201
		Enlisted Groundcrew	0.90 (0.52,1.56)	0.710
15-23	Femoral Pulses	All	1.91 (0.72,5.10)	0.193
		Officer	1.02 (0.25,4.22)	0.974
		Enlisted Flyer	6.47 (0.63,66.27)	0.115
		Enlisted Groundcrew	2.17 (0.34,13.80)	0.411
15-24	Popliteal Pulses	All	0.79 (0.40,1.55)	0.482
		Officer	0.64 (0.24,1.70)	0.374
		Enlisted Flyer	1.18 (0.30,4.68)	0.811
		Enlisted Groundcrew	0.80 (0.22,2.91)	0.731

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
15-25	Dorsalis Pedis Pulses	All	0.96 (0.67,1.38)	0.841
		Officer	0.81 (0.46,1.40)	0.442
		Enlisted Flyer	0.68 (0.29,1.61)	0.386
		Enlisted Groundcrew	1.37 (0.78,2.42)	0.275
15-26	Posterior Tibial Pulses	All	0.59 (0.36,0.95)	0.027
		Officer	0.46 (0.22,0.99)	0.047
		Enlisted Flyer	0.79 (0.26,2.35)	0.668
		Enlisted Groundcrew	0.66 (0.30,1.42)	0.284
15-27	Leg Pulses	All	0.82 (0.58,1.17)	0.274
		Officer	0.65 (0.38,1.11)	0.117
		Enlisted Flyer	0.78 (0.34,1.82)	0.567
		Enlisted Groundcrew	1.09 (0.63,1.90)	0.754
15-28	Peripheral Pulses	All	0.89 (0.68,1.16)	0.390
		Officer	0.80 (0.53,1.22)	0.300
		Enlisted Flyer	0.65 (0.33,1.29)	0.220
		Enlisted Groundcrew	1.11 (0.73,1.67)	0.631
15-30	Resting Pressure Index	All	1.00 (0.59,1.71)	0.986
		Officer	0.83 (0.38,1.79)	0.628
		Enlisted Flyer	1.30 (0.41,4.11)	0.654
		Enlisted Groundcrew	1.15 (0.45,2.93)	0.777
15-32	Hyperemic Pressure Index (1 Minute Post-exercise)	All	1.02 (0.72,1.47)	0.896
		Officer	0.76 (0.40,1.42)	0.383
		Enlisted Flyer	1.53 (0.74,3.14)	0.252
		Enlisted Groundcrew	1.04 (0.60,1.79)	0.899
15-34	Hyperemic Pressure Index (2 Minutes Post-exercise)	All	0.78 (0.48,1.25)	0.293
		Officer	0.54 (0.25,1.19)	0.129
		Enlisted Flyer	0.84 (0.31,2.27)	0.735
		Enlisted Groundcrew	1.05 (0.50,2.22)	0.892
15-35	Intermittent Claudication and Vascular Insufficiency Index	All	0.83 (0.47,1.46)	0.505
		Officer	0.81 (0.31,2.10)	0.662
		Enlisted Flyer	1.15 (0.29,4.47)	0.844
		Enlisted Groundcrew	0.75 (0.32,1.71)	0.488
16-13	RBC Morphology	All	1.36 (0.92,2.01)	0.131
		Officer	0.87 (0.47,1.60)	0.658
		Enlisted Flyer	1.55 (0.61,3.97)	0.359
		Enlisted Groundcrew	2.10 (1.12,3.97)	0.022
16-16	Absolute Neutrophils (Bands) (Zero vs. Nonzero)	All	0.92 (0.73,1.16)	0.471
		Officer	0.82 (0.56,1.20)	0.310
		Enlisted Flyer	0.79 (0.45,1.38)	0.401
		Enlisted Groundcrew	1.07 (0.76,1.51)	0.698
16-20	Absolute Eosinophils (Zero vs. Nonzero)	All	0.86 (0.63,1.17)	0.340
		Officer	0.73 (0.44,1.20)	0.212
		Enlisted Flyer	1.15 (0.53,2.48)	0.728
		Enlisted Groundcrew	0.90 (0.58,1.41)	0.650

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
16-22	Absolute Basophils (Zero vs. Nonzero)	All	1.06 (0.88,1.27)	0.521
		Officer	0.91 (0.68,1.22)	0.546
		Enlisted Flyer	0.94 (0.60,1.47)	0.774
		Enlisted Groundcrew	1.27 (0.97,1.68)	0.086
16-24	Fibrinogen	All	1.19 (0.80,1.76)	0.396
		Officer	1.55 (0.76,3.17)	0.228
		Enlisted Flyer	0.98 (0.44,2.18)	0.968
		Enlisted Groundcrew	1.10 (0.61,1.97)	0.755
16-26	Erythrocyte Sedimentation Rate	All	1.22 (0.91,1.65)	0.191
		Officer	1.37 (0.82,2.29)	0.230
		Enlisted Flyer	1.40 (0.71,2.76)	0.325
		Enlisted Groundcrew	1.06 (0.68,1.66)	0.796
17-3	Occurrence of Kidney Stones	All	1.09 (0.81,1.47)	0.558
		Officer	1.37 (0.88,2.14)	0.169
		Enlisted Flyer	0.98 (0.48,1.99)	0.961
		Enlisted Groundcrew	0.89 (0.55,1.44)	0.634
17-4	Occurrence of Past Kidney Disease	All	0.90 (0.75,1.10)	0.311
		Officer	0.88 (0.65,1.21)	0.436
		Enlisted Flyer	1.30 (0.81,2.08)	0.280
		Enlisted Groundcrew	0.81 (0.60,1.08)	0.147
17-9	Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero vs. Zero)	All	1.18 (0.90,1.56)	0.238
		Officer	1.03 (0.63,1.68)	0.904
		Enlisted Flyer	1.71 (0.91,3.23)	0.097
		Enlisted Groundcrew	1.12 (0.75,1.67)	0.582
17-11	Urinary Occult Blood	All	1.36 (0.76,2.43)	0.308
		Officer	2.20 (0.93,5.22)	0.073
		Enlisted Flyer	0.92 (0.15,5.59)	0.925
		Enlisted Groundcrew	0.87 (0.34,2.20)	0.761
17-12	Urinary WBC Count	All	1.32 (0.91,1.92)	0.145
		Officer	1.11 (0.59,2.08)	0.748
		Enlisted Flyer	1.40 (0.48,4.12)	0.538
		Enlisted Groundcrew	1.47 (0.88,2.46)	0.143
17-13	Urinary Protein	All	0.81 (0.50,1.34)	0.416
		Officer	0.73 (0.29,1.86)	0.513
		Enlisted Flyer	0.98 (0.30,3.23)	0.978
		Enlisted Groundcrew	0.82 (0.42,1.59)	0.549
18-3	Past Thyroid Disease	All	0.80 (0.61,1.07)	0.133
		Officer	0.89 (0.57,1.39)	0.607
		Enlisted Flyer	0.79 (0.39,1.59)	0.505
		Enlisted Groundcrew	0.74 (0.47,1.14)	0.173
18-4	Composite Diabetes Indicator (2002 AFHS Diabetes Definition)	All	0.93 (0.72,1.19)	0.567
		Officer	0.89 (0.59,1.35)	0.590
		Enlisted Flyer	0.93 (0.52,1.66)	0.799
		Enlisted Groundcrew	0.96 (0.66,1.40)	0.840

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
18-5	Composite Diabetes Indicator (Pre-2002 AFHS Diabetes Definition)	All	0.91 (0.72,1.16)	0.442
		Officer	1.07 (0.72,1.58)	0.753
		Enlisted Flyer	0.78 (0.45,1.37)	0.387
		Enlisted Groundcrew	0.85 (0.59,1.22)	0.381
18-8	Time to Diabetes Onset (2002 AFHS Diabetes Definition)	All	0.92 (0.75,1.15)[a]	0.468[a]
		Officer	0.90 (0.63,1.29)[a]	0.580[a]
		Enlisted Flyer	0.89 (0.54,1.45)[a]	0.630[a]
		Enlisted Groundcrew	0.96 (0.70,1.32)[a]	0.800[a]
18-9	Time to Diabetes Onset (Pre-2002 AFHS Diabetes Definition)	All	0.89 (0.73,1.09)[a]	0.246[a]
		Officer	0.99 (0.71,1.39)[a]	0.969[a]
		Enlisted Flyer	0.75 (0.47,1.21)[a]	0.240[a]
		Enlisted Groundcrew	0.87 (0.65,1.18)[a]	0.379[a]
18-10	Thyroid Gland	All	0.50 (0.22,1.11)	0.073
		Officer	0.55 (0.14,2.08)	0.375
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.59 (0.21,1.68)	0.324
18-11	Testicular Examination	All	1.09 (0.76,1.56)	0.647
		Officer	0.92 (0.52,1.63)	0.780
		Enlisted Flyer	1.47 (0.66,3.27)	0.345
		Enlisted Groundcrew	1.11 (0.62,1.98)	0.736
18-15	Free T_4	All	0.87 (0.63,1.19)	0.373
		Officer	1.21 (0.72,2.03)	0.469
		Enlisted Flyer	0.37 (0.15,0.89)	0.026
		Enlisted Groundcrew	0.88 (0.55,1.40)	0.585
18-16	Anti-thyroid Antibodies	All	0.98 (0.27,3.49)	0.974
		Officer	0.99 (0.16,5.99)	0.994
		Enlisted Flyer	2.84 (0.25,31.70)	0.396
		Enlisted Groundcrew	--	--
18-18	Fasting Glucose	All	1.09 (0.86,1.38)	0.469
		Officer	1.05 (0.71,1.54)	0.819
		Enlisted Flyer	0.96 (0.55,1.68)	0.882
		Enlisted Groundcrew	1.19 (0.84,1.70)	0.332
18-20	2-hour Postprandial Glucose (Nondiabetics Only)	All	1.00 (0.77,1.29)	0.992
		Officer	1.34 (0.88,2.03)	0.172
		Enlisted Flyer	1.02 (0.56,1.83)	0.958
		Enlisted Groundcrew	0.77 (0.52,1.15)	0.201
18-21	2-hour Postprandial Urinary Glucose (Nondiabetics Only)	All	1.07 (0.85,1.35)	0.583
		Officer	1.48 (1.00,2.20)	0.050
		Enlisted Flyer	1.02 (0.59,1.77)	0.940
		Enlisted Groundcrew	0.86 (0.61,1.20)	0.367
18-27	Hemoglobin A1c (Diabetics Only)	All	0.97 (0.61,1.54)	0.907
		Officer	0.84 (0.41,1.74)	0.644
		Enlisted Flyer	0.73 (0.25,2.13)	0.560
		Enlisted Groundcrew	1.28 (0.61,2.68)	0.507

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
18-29	C-peptide (Diabetics Only)	All	1.04 (0.61,1.80)	0.875
		Officer	1.63 (0.65,4.07)	0.295
		Enlisted Flyer	0.53 (0.13,2.21)	0.381
		Enlisted Groundcrew	0.94 (0.42,2.06)	0.868
18-31	Proinsulin (Diabetics Only)	All	1.27 (0.79,2.06)	0.323
		Officer	1.69 (0.76,3.78)	0.199
		Enlisted Flyer	0.44 (0.14,1.37)	0.155
		Enlisted Groundcrew	1.57 (0.77,3.22)	0.219
18-32	GADA (Diabetics Only)	All	0.53 (0.14,1.98)	0.321
		Officer	1.05 (0.17,6.57)	0.961
		Enlisted Flyer	--	--
		Enlisted Groundcrew	0.41 (0.04,3.81)	0.434
18-34	Total Testosterone	All	1.18 (0.91,1.54)	0.207
		Officer	1.31 (0.87,1.98)	0.200
		Enlisted Flyer	1.17 (0.61,2.24)	0.643
		Enlisted Groundcrew	1.08 (0.73,1.61)	0.688
18-36	Free Testosterone	All	1.10 (0.74,1.64)	0.633
		Officer	1.87 (1.03,3.39)	0.039
		Enlisted Flyer	0.65 (0.27,1.54)	0.326
		Enlisted Groundcrew	0.75 (0.36,1.55)	0.439
18-38	Estradiol	All	1.16 (0.67,2.01)	0.608
		Officer	1.67 (0.70,3.99)	0.247
		Enlisted Flyer	0.33 (0.07,1.59)	0.166
		Enlisted Groundcrew	1.32 (0.56,3.10)	0.522
18-40	LH	All	0.74 (0.48,1.13)	0.155
		Officer	0.71 (0.37,1.39)	0.318
		Enlisted Flyer	0.61 (0.22,1.68)	0.336
		Enlisted Groundcrew	0.83 (0.43,1.61)	0.582
18-42	FSH	All	0.92 (0.62,1.37)	0.692
		Officer	1.22 (0.70,2.11)	0.481
		Enlisted Flyer	0.75 (0.31,1.80)	0.523
		Enlisted Groundcrew	0.63 (0.28,1.40)	0.255
19-14	Lupus Panel: ANA Test	All	0.99 (0.77,1.27)	0.946
		Officer	0.87 (0.59,1.27)	0.461
		Enlisted Flyer	1.01 (0.53,1.91)	0.978
		Enlisted Groundcrew	1.12 (0.77,1.62)	0.548
19-15	Lupus Panel: Thyroid Microsomal Antibody	All	1.56 (0.86,2.80)	0.143
		Officer	1.48 (0.59,3.72)	0.407
		Enlisted Flyer	0.74 (0.13,4.18)	0.736
		Enlisted Groundcrew	1.97 (0.83,4.68)	0.122
19-16	Lupus Panel: MSK Antismooth Muscle Antibody	All	1.90 (0.71,5.02)	0.199
		Officer	5.27 (1.04,26.82)	0.045
		Enlisted Flyer	0.46 (0.05,4.69)	0.516
		Enlisted Groundcrew	1.20 (0.19,7.42)	0.845

Table Ref.	Clinical Parameter	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
19-17	Lupus Panel: MSK Antimitochondrial Antibody	All	1.48 (0.20,10.71)	0.699
		Officer	3.02 (0.27,33.73)	0.369
		Enlisted Flyer	--	--
		Enlisted Groundcrew	--	--
19-18	Lupus Panel: MSK Antiparietal Cell Antibody	All	0.73 (0.40,1.35)	0.310
		Officer	1.72 (0.62,4.84)	0.300
		Enlisted Flyer	0.25 (0.03,2.18)	0.209
		Enlisted Groundcrew	0.52 (0.22,1.25)	0.142
19-19	Lupus Panel: Rheumatoid Factor	All	1.25 (0.99,1.58)	0.059
		Officer	1.55 (1.05,2.28)	0.028
		Enlisted Flyer	0.91 (0.52,1.59)	0.749
		Enlisted Groundcrew	1.20 (0.85,1.69)	0.293
20-3	Asthma	All	1.01 (0.70,1.46)	0.959
		Officer	1.09 (0.61,1.96)	0.761
		Enlisted Flyer	0.43 (0.15,1.23)	0.115
		Enlisted Groundcrew	1.24 (0.72,2.16)	0.440
20-4	Bronchitis	All	1.06 (0.86,1.29)	0.596
		Officer	0.96 (0.69,1.32)	0.792
		Enlisted Flyer	1.45 (0.89,2.37)	0.135
		Enlisted Groundcrew	1.02 (0.76,1.38)	0.900
20-5	Pneumonia	All	0.91 (0.69,1.20)	0.509
		Officer	0.87 (0.57,1.34)	0.535
		Enlisted Flyer	1.94 (1.01,3.72)	0.046
		Enlisted Groundcrew	0.69 (0.45,1.06)	0.093
20-6	Thorax and Lung Abnormality	All	1.18 (0.90,1.54)	0.226
		Officer	1.07 (0.67,1.70)	0.793
		Enlisted Flyer	1.55 (0.87,2.77)	0.141
		Enlisted Groundcrew	1.12 (0.76,1.66)	0.569
20-7	X-ray Interpretation	All	0.84 (0.65,1.07)	0.160
		Officer	0.76 (0.51,1.14)	0.192
		Enlisted Flyer	1.13 (0.64,2.00)	0.679
		Enlisted Groundcrew	0.80 (0.54,1.17)	0.246
20-9	FVC	All	0.91 (0.66,1.26)	0.566
		Officer	0.99 (0.56,1.76)	0.986
		Enlisted Flyer	0.75 (0.37,1.56)	0.448
		Enlisted Groundcrew	0.93 (0.58,1.48)	0.751
20-11	FEV_1	All	1.06 (0.86,1.31)	0.564
		Officer	1.14 (0.81,1.60)	0.445
		Enlisted Flyer	1.24 (0.76,2.02)	0.393
		Enlisted Groundcrew	0.94 (0.68,1.29)	0.687

[a]Hazard ratio, confidence interval, and p-value, based on proportional hazards model, were given for time to diabetes onset variable.

--: Relative risk, confidence interval, and p-value were not presented because of the sparse number of participants with abnormalities.

Table G-18. Summary of Adjusted Results for Dichotomous Variables – Model 2 (Ranch Hands: Log$_2$ (Initial Dioxin))

Table Ref.	Clinical Parameter	Adjusted Relative Risk (95% C.I.)[a]		p-Value
9-3	Self-perception of Health	1.16	(0.91,1.47)	0.224
9-4	Appearance of Illness or Distress	1.12	(0.70,1.79)	0.631
9-5	Relative Age Appearance	1.00	(0.74,1.34)	0.975
9-7	Body Mass Index	1.03	(0.86,1.23)	0.744
10-3	All Skin Neoplasms	0.91	(0.75,1.10)	0.313
10-4	Malignant Skin Neoplasms	0.96	(0.76,1.20)	0.693
10-5	Benign Skin Neoplasms	0.91	(0.76,1.09)	0.296
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	0.23	(0.04,1.38)	0.033
10-7	Basal Cell Carcinoma	0.88	(0.68,1.13)	0.309
10-8	Squamous Cell Carcinoma	0.96	(0.63,1.46)	0.861
10-9	Nonmelanoma	0.92	(0.73,1.16)	0.484
10-10	Melanoma	1.07	(0.66,1.74)	0.788
10-11	Systemic Neoplasms	0.99	(0.82,1.20)	0.938
10-12	Malignant Systemic Neoplasms	0.98	(0.72,1.33)	0.898
10-13	Benign Systemic Neoplasms	0.99	(0.81,1.22)	0.939
10-14	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	1.13	(0.57,2.24)	0.736
10-16	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	2.62	(0.67,10.23)	0.155
10-17	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	0.12	(0.01,1.09)	0.010
10-18	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	--		--
10-19	Malignant Systemic Neoplasms (Thyroid Gland)	0.19	(0.01,6.92)	0.218
10-20	Malignant Systemic Neoplasms (Bronchus and Lung)	0.87	(0.44,1.71)	0.673
10-21	All Stomach Neoplasms	1.70	(0.69,4.24)	0.245
10-22	Malignant Systemic Neoplasms (Colon and Rectum)	1.03	(0.52,2.05)	0.924
10-23	Malignant Systemic Neoplasms (Urinary System)	2.08	(0.99,4.37)	0.049
10-24	Malignant Systemic Neoplasms (Kidney and Ureter)	1.89	(0.38,9.43)	0.426
10-25	Malignant Systemic Neoplasms (Prostate)	0.67	(0.43,1.05)	0.069
10-26	Malignant Systemic Neoplasms (Penis and Other Male Genital Organs)	2.93	(0.82,10.42)	0.058
10-27	Malignant Systemic Neoplasms (Testicles)	0.75	(0.23,2.44)	0.615
10-28	Malignant Systemic Neoplasms (Bone and Articular Cartilage)	--		--
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	2.62	(0.67,10.23)	0.155
10-30	Carcinoma in Situ	0.41	(0.09,1.91)	0.177
10-31	Hodgkin's Disease	--		--
10-32	Leukemia	--		--
10-33	Other Malignant Systemic Neoplasms (Lymphoid and Histiocytic Tissue)	0.83	(0.33,2.13)	0.697
10-34	Lymphoreticular Sarcoma	--		--
10-35	Skin and Systemic Neoplasms	0.91	(0.75,1.11)	0.372
10-36	Malignant Skin and Systemic Neoplasms	0.93	(0.75,1.16)	0.540
10-38	PSA	0.60	(0.34,1.06)	0.058
11-3	Inflammatory Diseases	1.01	(0.45,2.23)	0.989
11-4	Hereditary and Degenerative Diseases	1.06	(0.83,1.36)	0.654
11-5	Peripheral Disorders	0.99	(0.81,1.22)	0.921
11-6	Other Neurological Disorders	1.05	(0.85,1.29)	0.664
11-7	Smell	0.30	(0.10,0.89)	0.007
11-8	Visual Fields	0.98	(0.43,2.24)	0.957
11-9	Light Reaction	4.09	(0.77,21.67)	0.057

Table Ref.	Clinical Parameter	Adjusted Relative Risk (95% C.I.)[a]		p-Value
11-10	Ocular Movement	0.19	(0.01,5.66)	0.189
11-11	Facial Sensation	0.43	(0.08,2.40)	0.276
11-12	Corneal Reflex	0.73	(0.03,15.84)	0.831
11-13	Smile	0.86	(0.40,1.83)	0.686
11-14	Palpebral Fissure	1.51	(0.86,2.65)	0.155
11-15	Balance	2.11	(1.03,4.34)	0.033
11-16	Gag Reflex	0.58	(0.09,3.82)	0.490
11-17	Speech	0.92	(0.34,2.48)	0.875
11-18	Tongue Position Relative to Midline	1.23	(0.36,4.24)	0.742
11-19	Shoulder Shrug	0.15	(0.01,3.33)	0.101
11-20	Cranial Nerve Index	0.99	(0.73,1.33)	0.926
11-21	Pinprick	1.26	(0.92,1.73)	0.155
11-22	Light Touch	1.32	(0.88,1.98)	0.174
11-23	Muscle Status	1.06	(0.73,1.56)	0.751
11-27	Babinski Reflex	1.48	(0.51,4.32)	0.481
11-28	Any Symmetric Peripheral Abnormality	1.06	(0.85,1.31)	0.610
11-29	Possible Peripheral Neuropathy	1.01	(0.81,1.26)	0.915
11-30	Probable Peripheral Neuropathy	1.26	(0.88,1.81)	0.198
11-31	Tremor	1.28	(0.91,1.82)	0.160
11-32	Coordination	2.25	(1.30,3.90)	0.002
11-33	Romberg Sign	2.11	(1.03,4.34)	0.033
11-34	Gait	0.94	(0.68,1.30)	0.728
11-35	CNS Index	1.09	(0.85,1.41)	0.498
12-3	Psychoses	0.94	(0.68,1.31)	0.715
12-4	Alcohol Dependence	1.01	(0.71,1.43)	0.961
12-5	Drug Dependence	--		--
12-6	Anxiety	0.94	(0.78,1.13)	0.497
12-7	Other Neuroses	0.95	(0.79,1.16)	0.626
12-8	SCL-90-R Anxiety	0.80	(0.60,1.06)	0.115
12-9	SCL-90-R Depression	0.95	(0.73,1.24)	0.713
12-10	SCL-90-R Hostility	1.09	(0.76,1.56)	0.646
12-11	SCL-90-R Interpersonal Sensitivity	1.05	(0.77,1.44)	0.745
12-12	SCL-90-R Obsessive-compulsive Behavior	1.06	(0.85,1.34)	0.589
12-13	SCL-90-R Paranoid Ideation	1.06	(0.67,1.67)	0.803
12-14	SCL-90-R Phobic Anxiety	0.93	(0.67,1.31)	0.688
12-15	SCL-90-R Psychoticism	1.15	(0.87,1.53)	0.325
12-16	SCL-90-R Somatization	1.16	(0.91,1.47)	0.226
12-17	SCL-90-R Global Severity	1.01	(0.77,1.31)	0.966
12-18	SCL-90-R Positive Symptom Total	0.96	(0.72,1.28)	0.778
12-19	SCL-90-R Positive Symptom Distress Index	1.05	(0.78,1.42)	0.727
13-3	Uncharacterized Hepatitis	1.10	(0.64,1.89)	0.738
13-4	Jaundice	0.97	(0.33,2.86)	0.951
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	1.28	(0.83,1.97)	0.272
13-6	Chronic Liver Disease and Cirrhosis (Nonalcohol-related)	1.22	(0.78,1.90)	0.377
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	1.63	(0.67,3.96)	0.297
13-8	Enlarged Liver	0.78	(0.49,1.25)	0.286
13-9	Other Disorders of the Liver	1.04	(0.87,1.23)	0.687
13-10	Current Hepatomegaly	0.73	(0.38,1.42)	0.337
13-12	AST	1.24	(0.87,1.77)	0.229

Table Ref.	Clinical Parameter	Adjusted Relative Risk (95% C.I.)[a]		p-Value
13-14	ALT	1.20	(0.85,1.70)	0.288
13-16	GGT	0.87	(0.63,1.21)	0.402
13-18	Alkaline Phosphatase	1.06	(0.79,1.42)	0.701
13-20	Total Bilirubin	0.92	(0.62,1.37)	0.674
13-21	Direct Bilirubin	--		--
13-23	LDH	0.84	(0.62,1.13)	0.240
13-25	Cholesterol	1.08	(0.80,1.46)	0.635
13-27	HDL Cholesterol	0.91	(0.73,1.12)	0.366
13-29	Cholesterol-HDL Ratio	0.93	(0.77,1.12)	0.430
13-31	Triglycerides	1.06	(0.85,1.33)	0.577
13-33	Creatine Phosphokinase	0.92	(0.67,1.27)	0.620
13-35	Serum Amylase	0.70	(0.42,1.20)	0.181
13-36	Antibodies for Hepatitis A	1.05	(0.87,1.27)	0.582
13-37	Serological Evidence of Prior Hepatitis B Infection	1.07	(0.79,1.44)	0.666
13-38	Antibodies for Hepatitis C	0.23	(0.03,1.94)	0.078
13-39	Stool Hemoccult	1.04	(0.48,2.24)	0.918
13-41	Prealbumin	1.09	(0.63,1.88)	0.768
13-43	Albumin	--		--
13-45	α-1-Acid Glycoprotein	0.76	(0.54,1.08)	0.111
13-49	α-2-Macroglobulin	1.06	(0.82,1.38)	0.638
13-51	Apolipoprotein B	1.18	(0.50,2.82)	0.707
13-53	C3 Complement	2.83	(0.19,42.52)	0.442
13-55	C4 Complement	1.80	(1.26,2.57)	<0.001
13-57	Haptoglobin	0.75	(0.58,0.97)	0.026
13-59	Transferrin	1.36	(0.86,2.15)	0.187
13-61	Prothrombin Time	0.38	(0.09,1.58)	0.137
14-3	Acne (Lifetime)	0.84	(0.71,1.00)	0.052
14-4	Post-SEA Acne	0.92	(0.76,1.11)	0.382
14-5	Post-SEA Acne (No Pre-SEA Acne)	0.88	(0.69,1.14)	0.331
14-6	Post-SEA Acne (with Pre-SEA Acne)	1.10	(0.79,1.53)	0.557
14-8	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (Excluding Participants with Pre-SEA Acne)	1.32	(0.86,2.02)	0.196
14-10	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (All Post-SEA Occurrences)	1.06	(0.76,1.47)	0.728
14-13	Acneiform Lesions	1.14	(0.80,1.63)	0.467
14-14	Acneiform Scars	1.03	(0.71,1.49)	0.877
14-15	Comedones	1.44	(1.00,2.09)	0.052
14-16	Depigmentation	1.21	(0.71,2.04)	0.492
14-17	Hyperpigmentation	0.77	(0.56,1.07)	0.108
14-18	Inclusion Cysts	1.09	(0.85,1.40)	0.485
14-19	Dermatology Index	1.17	(0.96,1.42)	0.115
15-3	Essential Hypertension	1.12	(0.91,1.37)	0.292
15-4	Heart Disease (Excluding Essential Hypertension)	1.08	(0.85,1.38)	0.524
15-5	Myocardial Infarction	1.31	(0.97,1.77)	0.082
15-6	Stroke or Transient Ischemic Attack	1.26	(0.78,2.03)	0.336
15-8	Systolic Blood Pressure	0.91	(0.72,1.13)	0.388
15-10	Diastolic Blood Pressure	1.18	(0.81,1.72)	0.395
15-11	Heart Sounds	0.97	(0.67,1.40)	0.867
15-12	Overall ECG	1.05	(0.86,1.29)	0.609

Table Ref.	Clinical Parameter	Adjusted Relative Risk (95% C.I.)[a]	p-Value
15-13	ECG: RBBB	1.17 (0.69,1.97)	0.567
15-14	ECG: LBBB	2.19 (0.49,9.86)	0.271
15-15	ECG: Nonspecific ST- and T-wave Changes	1.14 (0.91,1.43)	0.246
15-16	ECG: Bradycardia	1.03 (0.62,1.72)	0.914
15-17	ECG: Tachycardia	5.69 (0.24,134.10)	0.132
15-18	ECG: Arrhythmia	0.74 (0.51,1.06)	0.092
15-19	ECG: Evidence of Prior Myocardial Infarction	1.57 (0.96,2.59)	0.071
15-20	Funduscopic Examination	1.09 (0.80,1.47)	0.590
15-21	Carotid Bruits	2.34 (0.86,6.38)	0.079
15-22	Radial Pulses	1.18 (0.78,1.78)	0.443
15-23	Femoral Pulses	0.84 (0.37,1.91)	0.681
15-24	Popliteal Pulses	0.88 (0.45,1.70)	0.694
15-25	Dorsalis Pedis Pulses	1.14 (0.82,1.58)	0.430
15-26	Posterior Tibial Pulses	1.64 (0.94,2.84)	0.072
15-27	Leg Pulses	1.19 (0.86,1.64)	0.300
15-28	Peripheral Pulses	1.28 (0.98,1.67)	0.074
15-30	Resting Pressure Index	1.37 (0.80,2.32)	0.246
15-32	Hyperemic Pressure Index (1 Minute Post-exercise)	1.12 (0.78,1.59)	0.545
15-34	Hyperemic Pressure Index (2 Minutes Post-exercise)	1.13 (0.62,2.03)	0.696
15-35	Intermittent Claudication and Vascular Insufficiency Index	1.33 (0.77,2.29)	0.308
16-13	RBC Morphology	1.13 (0.81,1.59)	0.476
16-16	Absolute Neutrophils (Bands) (Zero vs. Nonzero)	0.99 (0.80,1.24)	0.963
16-20	Absolute Eosinophils (Zero vs. Nonzero)	0.99 (0.74,1.32)	0.955
16-22	Absolute Basophils (Zero vs. Nonzero)	0.99 (0.84,1.18)	0.939
16-24	Fibrinogen	1.03 (0.75,1.42)	0.862
16-26	Erythrocyte Sedimentation Rate	1.09 (0.84,1.40)	0.531
17-3	Occurrence of Kidney Stones	0.76 (0.57,1.02)	0.059
17-4	Occurrence of Past Kidney Disease	1.12 (0.93,1.34)	0.238
17-9	Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero vs. Zero)	0.88 (0.69,1.12)	0.284
17-11	Urinary Occult Blood	1.00 (0.56,1.78)	0.995
17-12	Urinary WBC Count	1.07 (0.78,1.46)	0.681
17-13	Urinary Protein	0.88 (0.57,1.37)	0.566
18-3	Past Thyroid Disease	1.16 (0.87,1.53)	0.321
18-4	Composite Diabetes Indicator (2002 AFHS Diabetes Definition)	1.25 (0.99,1.58)	0.061
18-5	Composite Diabetes Indicator (Pre-2002 AFHS Diabetes Definition)	1.34 (1.07,1.68)	0.010
18-8	Time to Diabetes Onset (2002 AFHS Diabetes Definition)	1.20 (1.00,1.45)[b]	0.055[b]
18-9	Time to Diabetes Onset (Pre-2002 AFHS Diabetes Definition)	1.21 (1.02,1.45)[b]	0.033[b]
18-10	Thyroid Gland	0.27 (0.04,1.84)	0.094
18-11	Testicular Examination	1.34 (0.97,1.85)	0.073
18-15	Free T$_4$	1.00 (0.75,1.34)	0.998
18-16	Anti-thyroid Antibodies	0.84 (0.30,2.33)	0.724
18-18	Fasting Glucose	1.09 (0.88,1.35)	0.409
18-20	2-hour Postprandial Glucose (Nondiabetics Only)	0.80 (0.61,1.04)	0.094
18-21	2-hour Postprandial Urinary Glucose (Nondiabetics Only)	1.05 (0.83,1.33)	0.678
18-27	Hemoglobin A1c (Diabetics Only)	1.51 (0.96,2.36)	0.060
18-29	C-peptide (Diabetics Only)	0.63 (0.37,1.07)	0.067
18-31	Proinsulin (Diabetics Only)	0.70 (0.46,1.05)	0.075
18-32	GADA (Diabetics Only)	1.11 (0.35,3.53)	0.859
18-34	Total Testosterone	0.95 (0.76,1.19)	0.650

Table Ref.	Clinical Parameter	Adjusted Relative Risk (95% C.I.)[a]	p-Value
18-35	Free Testosterone	1.14 (0.81,1.61)	0.459
18-38	Estradiol	1.54 (0.97,2.45)	0.077
18-40	LH	0.99 (0.66,1.51)	0.980
18-42	FSH	0.92 (0.61,1.39)	0.699
19-14	Lupus Panel: ANA Test	1.28 (1.02,1.61)	0.035
19-15	Lupus Panel: Thyroid Microsomal Antibody	0.84 (0.51,1.38)	0.483
19-16	Lupus Panel: MSK Antismooth Muscle Antibody	0.56 (0.17,1.89)	0.277
19-17	Lupus Panel: MSK Antimitochondrial Antibody	--	--
19-18	Lupus Panel: MSK Antiparietal Cell Antibody	1.16 (0.66,2.05)	0.608
19-19	Lupus Panel: Rheumatoid Factor	0.61 (0.47,0.78)	<0.001
20-3	Asthma	0.88 (0.60,1.28)	0.491
20-4	Bronchitis	1.07 (0.89,1.28)	0.500
20-5	Pneumonia	0.85 (0.65,1.12)	0.243
20-6	Thorax and Lung Abnormality	0.94 (0.74,1.18)	0.587
20-7	X-ray Interpretation	0.82 (0.64,1.06)	0.117
20-9	FVC	0.88 (0.66,1.18)	0.386
20-11	FEV$_1$	1.00 (0.82,1.21)	0.981

[a]Relative risk for a twofold increase in initial dioxin.
[b]Hazard ratio, confidence interval, and p-value, based on proportional hazards model, were given for time to diabetes onset variable.

--: Relative risk, confidence interval, and p-value were not presented because of the sparse number of Ranch Hands with abnormalities.

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
9-3	Self-perception of Health	Comparison	1,168		
		Background RH	351	1.04 (0.71,1.54)	0.841
		Low RH	210	0.97 (0.62,1.51)	0.879
		High RH	211	1.12 (0.74,1.69)	0.595
		Low plus High RH	421	1.04 (0.75,1.44)	0.817
9-4	Appearance of Illness or Distress	Comparison	1,168		
		Background RH	350	1.07 (0.57,2.03)	0.827
		Low RH	210	0.94 (0.46,1.93)	0.865
		High RH	211	0.77 (0.33,1.80)	0.545
		Low plus High RH	421	0.85 (0.47,1.54)	0.592
9-5	Relative Age Appearance	Comparison	1,168		
		Background RH	350	0.86 (0.42,1.79)	0.695
		Low RH	210	1.51 (0.78,2.92)	0.218
		High RH	211	1.45 (0.80,2.62)	0.223
		Low plus High RH	421	1.48 (0.91,2.41)	0.116
9-7	Body Mass Index	Comparison	1,168		
		Background RH	350	0.59 (0.45,0.79)	<0.001
		Low RH	210	1.48 (1.09,2.01)	0.011
		High RH	211	1.52 (1.11,2.07)	0.009
		Low plus High RH	421	1.50 (1.19,1.89)	0.001
10-3	All Skin Neoplasms	Comparison	1,081		
		Background RH	329	1.24 (0.96,1.60)	0.107
		Low RH	187	1.56 (1.13,2.17)	0.007
		High RH	202	1.13 (0.82,1.55)	0.465
		Low plus High RH	389	1.32 (1.03,1.68)	0.026
10-4	Malignant Skin Neoplasms	Comparison	1,081		
		Background RH	329	1.15 (0.84,1.56)	0.378
		Low RH	187	1.52 (1.06,2.19)	0.024
		High RH	202	1.06 (0.69,1.60)	0.801
		Low plus High RH	389	1.26 (0.93,1.70)	0.134
10-5	Benign Skin Neoplasms	Comparison	1,156		
		Background RH	347	1.25 (0.97,1.61)	0.091
		Low RH	208	1.25 (0.92,1.70)	0.155
		High RH	212	1.05 (0.76,1.44)	0.780
		Low plus High RH	420	1.14 (0.90,1.45)	0.272
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	Comparison	1,081		
		Background RH	329	2.60 (0.68,9.91)	0.162
		Low RH	187	4.14 (1.06,16.16)	0.041
		High RH	202	--	--
		Low plus High RH	389	--	--

Table G-19. Summary of Adjusted Results for Dichotomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
10-7	Basal Cell Carcinoma	Comparison	1,081		
		Background RH	329	1.32 (0.95,1.82)	0.098
		Low RH	187	1.66 (1.13,2.43)	0.010
		High RH	202	1.00 (0.63,1.58)	0.990
		Low plus High RH	389	1.27 (0.92,1.76)	0.145
10-8	Squamous Cell Carcinoma	Comparison	1,081		
		Background RH	329	0.91 (0.52,1.58)	0.728
		Low RH	187	1.25 (0.67,2.33)	0.480
		High RH	202	1.14 (0.52,2.49)	0.741
		Low plus High RH	389	1.19 (0.69,2.05)	0.524
10-9	Nonmelanoma	Comparison	1,081		
		Background RH	329	1.28 (0.94,1.74)	0.124
		Low RH	187	1.60 (1.10,2.31)	0.013
		High RH	202	1.06 (0.69,1.64)	0.783
		Low plus High RH	389	1.29 (0.95,1.76)	0.102
10-10	Melanoma	Comparison	1,081		
		Background RH	329	0.75 (0.33,1.68)	0.486
		Low RH	187	1.23 (0.52,2.90)	0.642
		High RH	202	1.01 (0.33,3.09)	0.980
		Low plus High RH	389	1.11 (0.52,2.38)	0.786
10-11	Systemic Neoplasms	Comparison	1,164		
		Background RH	348	0.90 (0.67,1.20)	0.471
		Low RH	203	1.27 (0.90,1.79)	0.174
		High RH	209	1.00 (0.69,1.45)	0.999
		Low plus High RH	412	1.12 (0.85,1.50)	0.418
10-12	Malignant Systemic Neoplasms	Comparison	1,166		
		Background RH	348	1.15 (0.74,1.80)	0.525
		Low RH	205	2.05 (1.28,3.26)	0.003
		High RH	210	1.09 (0.59,2.01)	0.778
		Low plus High RH	415	1.49 (0.96,2.30)	0.074
10-13	Benign Systemic Neoplasms	Comparison	1,164		
		Background RH	348	0.92 (0.67,1.26)	0.605
		Low RH	203	0.97 (0.67,1.41)	0.881
		High RH	209	1.02 (0.69,1.51)	0.903
		Low plus High RH	412	1.00 (0.74,1.35)	0.991
10-14	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	Comparison	1,166		
		Background RH	348	0.82 (0.34,1.99)	0.656
		Low RH	205	0.83 (0.29,2.36)	0.726
		High RH	210	0.37 (0.08,1.70)	0.201
		Low plus High RH	415	0.55 (0.20,1.50)	0.243
10-16	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	Comparison	1,166		
		Background RH	348	--	--
		Low RH	205	--	--
		High RH	210	0.99 (0.08,12.65)	0.991
		Low plus High RH	415	--	--

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
10-17	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	Comparison	1,166		
		Background RH	348	--	--
		Low RH	205	3.69 (0.81,16.83)	0.092
		High RH	210	--	--
		Low plus High RH	415	--	--
10-18	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	Comparison	1,166		
		Background RH	348	17.36 (0.45,664.89)	0.125
		Low RH	205	--	--
		High RH	210	--	--
		Low plus High RH	415	--	--
10-19	Malignant Systemic Neoplasms (Thyroid Gland)	Comparison	1,166		
		Background RH	348	--	--
		Low RH	205	2.90 (0.18,47.88)	0.456
		High RH	210	--	--
		Low plus High RH	415	--	--
10-20	Malignant Systemic Neoplasms (Bronchus and Lung)	Comparison	1,166		
		Background RH	348	1.30 (0.30,5.74)	0.728
		Low RH	205	3.91 (1.20,12.74)	0.024
		High RH	210	1.52 (0.27,8.64)	0.636
		Low plus High RH	415	2.42 (0.70,8.39)	0.162
10-21	All Stomach Neoplasms	Comparison	1,166		
		Background RH	348	0.80 (0.18,3.48)	0.767
		Low RH	205	0.81 (0.15,4.29)	0.802
		High RH	210	0.49 (0.05,4.61)	0.533
		Low plus High RH	415	0.63 (0.13,2.93)	0.553
10-22	Malignant Systemic Neoplasms (Colon and Rectum)	Comparison	1,166		
		Background RH	348	1.14 (0.26,5.06)	0.863
		Low RH	205	3.74 (1.10,12.73)	0.035
		High RH	210	1.21 (0.21,7.02)	0.831
		Low plus High RH	415	2.11 (0.60,7.40)	0.242
10-23	Malignant Systemic Neoplasms (Urinary System)	Comparison	1,166		
		Background RH	348	3.62 (1.24,10.51)	0.018
		Low RH	205	2.83 (0.81,9.88)	0.102
		High RH	210	2.20 (0.50,9.69)	0.296
		Low plus High RH	415	2.49 (0.79,7.83)	0.117
10-24	Malignant Systemic Neoplasms (Kidney and Ureter)	Comparison	1,166		
		Background RH	348	5.17 (0.88,30.37)	0.069
		Low RH	205	2.03 (0.17,24.09)	0.574
		High RH	210	1.33 (0.11,16.17)	0.822
		Low plus High RH	415	1.64 (0.22,12.31)	0.630

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
10-25	Malignant Systemic Neoplasms (Prostate)	Comparison	1,166		
		Background RH	348	1.03 (0.58,1.83)	0.928
		Low RH	205	1.85 (1.00,3.39)	0.048
		High RH	210	1.16 (0.51,2.62)	0.721
		Low plus High RH	415	1.46 (0.82,2.61)	0.202
10-26	Malignant Systemic Neoplasms (Penis and Other Male Genital Organs)	Comparison	1,166		
		Background RH	348	--	--
		Low RH	205	--	--
		High RH	210	--	--
		Low plus High RH	415	--	--
10-27	Malignant Systemic Neoplasms (Testicles)	Comparison	1,166		
		Background RH	348	--	--
		Low RH	205	--	--
		High RH	210	--	--
		Low plus High RH	415	--	--
10-28	Malignant Systemic Neoplasms (Bone and Articular Cartilage)	Comparison	1,166		
		Background RH	348	--	--
		Low RH	205	--	--
		High RH	210	--	--
		Low plus High RH	415	--	--
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	Comparison	1,166		
		Background RH	348	--	--
		Low RH	205	--	--
		High RH	210	0.95 (0.09,10.22)	0.966
		Low plus High RH	415	--	--
10-30	Carcinoma in Situ	Comparison	1,166		
		Background RH	348	3.23 (0.20,51.07)	0.405
		Low RH	205	20.75 (1.40,307.55)	0.027
		High RH	210	--	--
		Low plus High RH	415	--	--
10-31	Hodgkin's Disease	Comparison	1,166		
		Background RH	348	3.10 (0.18,53.55)	0.437
		Low RH	205	--	--
		High RH	210	--	--
		Low plus High RH	415	--	--
10-32	Leukemia	Comparison	1,166		
		Background RH	348	2.06 (0.42,10.04)	0.371
		Low RH	205	--	--
		High RH	210	--	--
		Low plus High RH	415	--	--
10-33	Other Malignant Systemic Neoplasms (Lymphoid and Histiocytic Tissue)	Comparison	1,166		
		Background RH	348	0.31 (0.04,2.65)	0.283
		Low RH	205	1.56 (0.42,5.85)	0.508
		High RH	210	0.39 (0.04,3.55)	0.404
		Low plus High RH	415	0.77 (0.19,3.22)	0.725

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]		p-Value
10-34	Lymphoreticular Sarcoma	Comparison	1,166			
		Background RH	348	1.05	(0.08,13.63)	0.973
		Low RH	205	--		--
		High RH	210	--		--
		Low plus High RH	415	--		--
10-35	Skin and Systemic Neoplasms	Comparison	1,148			
		Background RH	344	1.02	(0.76,1.37)	0.913
		Low RH	201	1.46	(1.00,2.12)	0.048
		High RH	208	0.94	(0.66,1.34)	0.727
		Low plus High RH	409	1.17	(0.87,1.56)	0.299
10-36	Malignant Skin and Systemic Neoplasms	Comparison	1,150			
		Background RH	344	1.01	(0.73,1.38)	0.969
		Low RH	202	1.64	(1.14,2.37)	0.008
		High RH	209	0.91	(0.60,1.38)	0.658
		Low plus High RH	411	1.22	(0.89,1.67)	0.219
10-38	PSA	Comparison	1,083			
		Background RH	323	0.91	(0.46,1.77)	0.773
		Low RH	187	1.57	(0.75,3.30)	0.230
		High RH	199	0.95	(0.34,2.69)	0.926
		Low plus High RH	386	1.21	(0.59,2.48)	0.596
11-3	Inflammatory Diseases	Comparison	1,156			
		Background RH	350	3.09	(0.92,10.34)	0.068
		Low RH	210	1.97	(0.39,9.97)	0.414
		High RH	208	1.74	(0.34,8.87)	0.506
		Low plus High RH	418	1.85	(0.52,6.60)	0.344
11-4	Hereditary and Degenerative Diseases	Comparison	1,164			
		Background RH	350	1.28	(0.91,1.80)	0.158
		Low RH	210	1.15	(0.76,1.73)	0.510
		High RH	208	1.13	(0.73,1.75)	0.572
		Low plus High RH	418	1.14	(0.83,1.58)	0.424
11-5	Peripheral Disorder	Comparison	1,161			
		Background RH	348	1.04	(0.77,1.40)	0.802
		Low RH	210	1.10	(0.78,1.55)	0.603
		High RH	208	0.96	(0.66,1.38)	0.815
		Low plus High RH	418	1.02	(0.78,1.34)	0.860
11-6	Other Neurological Disorders	Comparison	1,161			
		Background RH	348	1.03	(0.72,1.48)	0.873
		Low RH	210	1.18	(0.80,1.73)	0.417
		High RH	208	1.27	(0.87,1.85)	0.217
		Low plus High RH	418	1.22	(0.91,1.64)	0.186
11-7	Smell	Comparison	1,163			
		Background RH	350	1.80	(0.89,3.64)	0.103
		Low RH	210	1.57	(0.69,3.57)	0.286
		High RH	208	--		--
		Low plus High RH	418	--		--

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
11-8	Visual Fields	Comparison	1,152		
		Background RH	349	5.25 (1.71,16.13)	0.004
		Low RH	208	1.61 (0.31,8.30)	0.568
		High RH	207	1.72 (0.32,9.24)	0.526
		Low plus High RH	415	1.67 (0.45,6.19)	0.445
11-9	Light Reaction	Comparison	1,160		
		Background RH	349	1.11 (0.29,4.35)	0.877
		Low RH	210	--	--
		High RH	208	0.79 (0.10,6.63)	0.832
		Low plus High RH	418	--	--
11-10	Ocular Movement	Comparison	1,161		
		Background RH	349	2.94 (0.60,14.47)	0.185
		Low RH	210	1.72 (0.18,16.14)	0.633
		High RH	208	1.31 (0.11,16.31)	0.834
		Low plus High RH	418	1.50 (0.24,9.36)	0.662
11-11	Facial Sensation	Comparison	1,164		
		Background RH	350	1.33 (0.11,15.68)	0.823
		Low RH	210	7.94 (1.19,53.10)	0.033
		High RH	208	--	--
		Low plus High RH	418	--	--
11-12	Corneal Reflex	Comparison	1,157		
		Background RH	349	0.55 (0.06,5.01)	0.598
		Low RH	210	--	--
		High RH	208	1.22 (0.11,12.96)	0.869
		Low plus High RH	418	--	--
11-13	Smile	Comparison	1,164		
		Background RH	350	0.58 (0.12,2.86)	0.506
		Low RH	210	1.78 (0.51,6.17)	0.367
		High RH	208	1.20 (0.22,6.40)	0.833
		Low plus High RH	418	1.46 (0.46,4.62)	0.521
11-14	Palpebral Fissure	Comparison	1,163		
		Background RH	350	1.66 (0.77,3.55)	0.193
		Low RH	210	1.62 (0.67,3.92)	0.285
		High RH	208	1.36 (0.48,3.82)	0.559
		Low plus High RH	418	1.49 (0.70,3.13)	0.299
11-15	Balance	Comparison	1,163		
		Background RH	349	1.00 (0.40,2.48)	0.998
		Low RH	210	1.10 (0.42,2.87)	0.841
		High RH	208	1.40 (0.48,4.14)	0.538
		Low plus High RH	418	1.24 (0.56,2.75)	0.590
11-16	Gag Reflex	Comparison	1,164		
		Background RH	350	--	--
		Low RH	210	18.43 (0.60,567.42)	0.096
		High RH	208	8.50 (0.29,250.29)	0.215
		Low plus High RH	418	12.54 (0.65,241.33)	0.094

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
11-17	Speech	Comparison	1,164		
		Background RH	350	1.65 (0.52,5.26)	0.395
		Low RH	210	1.29 (0.27,6.12)	0.750
		High RH	208	2.48 (0.60,10.22)	0.210
		Low plus High RH	418	1.78 (0.57,5.62)	0.323
11-18	Tongue Position Relative to Midline	Comparison	1,164		
		Background RH	350	--	--
		Low RH	210	5.40 (0.69,42.33)	0.109
		High RH	208	3.28 (0.22,48.44)	0.387
		Low plus High RH	418	4.22 (0.57,31.00)	0.158
11-19	Shoulder Shrug	Comparison	1,164		
		Background RH	350	0.70 (0.08,6.25)	0.746
		Low RH	210	2.13 (0.39,11.61)	0.384
		High RH	208	--	--
		Low plus High RH	418	--	--
11-20	Cranial Nerve Index	Comparison	1,152		
		Background RH	347	1.65 (1.09,2.50)	0.018
		Low RH	208	1.62 (1.00,2.61)	0.049
		High RH	208	1.05 (0.59,1.89)	0.862
		Low plus High RH	416	1.31 (0.87,1.97)	0.204
11-21	Pinprick	Comparison	980		
		Background RH	302	1.19 (0.73,1.93)	0.482
		Low RH	163	0.81 (0.43,1.52)	0.515
		High RH	169	1.71 (1.00,2.93)	0.050
		Low plus High RH	332	1.19 (0.76,1.85)	0.450
11-22	Light Touch	Comparison	980		
		Background RH	302	0.99 (0.53,1.85)	0.964
		Low RH	163	0.86 (0.40,1.86)	0.709
		High RH	169	1.42 (0.74,2.75)	0.291
		Low plus High RH	332	1.11 (0.65,1.92)	0.696
11-23	Muscle Status	Comparison	1,163		
		Background RH	346	1.00 (0.57,1.77)	0.989
		Low RH	210	1.09 (0.56,2.11)	0.794
		High RH	207	1.09 (0.55,2.16)	0.806
		Low plus High RH	417	1.09 (0.65,1.82)	0.741
11-27	Babinski Reflex	Comparison	1,160		
		Background RH	349	1.27 (0.45,3.61)	0.652
		Low RH	210	0.82 (0.23,2.91)	0.761
		High RH	208	0.44 (0.10,2.01)	0.292
		Low plus High RH	418	0.60 (0.21,1.72)	0.345
11-28	Any Symmetric Peripheral Abnormality	Comparison	1,120		
		Background RH	335	1.02 (0.73,1.42)	0.917
		Low RH	206	1.25 (0.86,1.80)	0.244
		High RH	201	1.24 (0.83,1.84)	0.295
		Low plus High RH	407	1.24 (0.93,1.66)	0.148

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
11-29	Possible Peripheral Neuropathy	Comparison	1,121		
		Background RH	335	1.00 (0.71,1.40)	0.981
		Low RH	206	1.24 (0.85,1.80)	0.269
		High RH	201	1.14 (0.76,1.71)	0.539
		Low plus High RH	407	1.19 (0.88,1.60)	0.263
11-30	Probable Peripheral Neuropathy	Comparison	1,121		
		Background RH	335	1.29 (0.77,2.18)	0.330
		Low RH	206	0.93 (0.51,1.68)	0.805
		High RH	200	1.40 (0.75,2.62)	0.290
		Low plus High RH	406	1.14 (0.71,1.81)	0.590
11-31	Tremor	Comparison	1,164		
		Background RH	350	0.94 (0.58,1.52)	0.790
		Low RH	210	0.60 (0.30,1.19)	0.142
		High RH	208	1.30 (0.75,2.24)	0.345
		Low plus High RH	418	0.88 (0.55,1.40)	0.594
11-32	Coordination	Comparison	1,163		
		Background RH	349	0.93 (0.51,1.70)	0.823
		Low RH	210	0.46 (0.19,1.11)	0.083
		High RH	207	0.80 (0.37,1.71)	0.559
		Low plus High RH	417	0.60 (0.33,1.12)	0.109
11-33	Romberg Sign	Comparison	1,163		
		Background RH	349	1.00 (0.40,2.48)	0.998
		Low RH	210	1.10 (0.42,2.87)	0.841
		High RH	208	1.40 (0.48,4.14)	0.538
		Low plus High RH	418	1.24 (0.56,2.75)	0.590
11-34	Gait	Comparison	1,164		
		Background RH	350	0.83 (0.50,1.36)	0.454
		Low RH	210	0.97 (0.57,1.67)	0.919
		High RH	208	1.22 (0.70,2.11)	0.481
		Low plus High RH	418	1.09 (0.72,1.65)	0.692
11-35	CNS Index	Comparison	1,164		
		Background RH	350	0.88 (0.61,1.27)	0.508
		Low RH	210	0.74 (0.47,1.15)	0.183
		High RH	208	1.06 (0.69,1.62)	0.796
		Low plus High RH	418	0.88 (0.64,1.23)	0.464
12-3	Psychoses	Comparison	1,166		
		Background RH	351	1.03 (0.59,1.80)	0.927
		Low RH	210	1.01 (0.53,1.94)	0.970
		High RH	207	0.89 (0.49,1.62)	0.707
		Low plus High RH	417	0.95 (0.59,1.52)	0.834
12-4	Alcohol Dependence	Comparison	1,136		
		Background RH	344	1.28 (0.76,2.16)	0.357
		Low RH	202	0.84 (0.41,1.74)	0.638
		High RH	207	0.95 (0.50,1.80)	0.875
		Low plus High RH	409	0.89 (0.53,1.50)	0.670

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
12-5	Drug Dependence	Comparison	1,166		
		Background RH	351	0.88 (0.14,5.61)	0.892
		Low RH	210	--	--
		High RH	207	--	--
		Low plus High RH	417	--	--
12-6	Anxiety	Comparison	1,132		
		Background RH	341	1.07 (0.80,1.43)	0.666
		Low RH	201	1.17 (0.83,1.63)	0.374
		High RH	204	0.95 (0.68,1.32)	0.767
		Low plus High RH	405	1.05 (0.82,1.35)	0.693
12-7	Other Neuroses	Comparison	1,125		
		Background RH	337	0.90 (0.69,1.17)	0.442
		Low RH	201	1.14 (0.83,1.57)	0.416
		High RH	203	1.11 (0.79,1.56)	0.552
		Low plus High RH	404	1.13 (0.88,1.44)	0.353
12-8	SCL-90-R Anxiety	Comparison	1,135		
		Background RH	342	0.76 (0.45,1.29)	0.312
		Low RH	201	1.01 (0.58,1.75)	0.976
		High RH	205	0.87 (0.53,1.44)	0.594
		Low plus High RH	406	0.94 (0.63,1.40)	0.751
12-9	SCL-90-R Depression	Comparison	1,135		
		Background RH	342	0.80 (0.52,1.23)	0.302
		Low RH	201	0.83 (0.50,1.37)	0.461
		High RH	205	0.94 (0.60,1.47)	0.797
		Low plus High RH	406	0.88 (0.62,1.27)	0.499
12-10	SCL-90-R Hostility	Comparison	1,135		
		Background RH	342	1.12 (0.62,2.00)	0.710
		Low RH	201	0.46 (0.18,1.19)	0.110
		High RH	205	1.15 (0.65,2.02)	0.634
		Low plus High RH	406	0.73 (0.41,1.30)	0.289
12-11	SCL-90-R Interpersonal Sensitivity	Comparison	1,135		
		Background RH	342	0.71 (0.44,1.15)	0.163
		Low RH	201	0.40 (0.20,0.81)	0.011
		High RH	205	0.79 (0.48,1.31)	0.358
		Low plus High RH	406	0.56 (0.36,0.88)	0.013
12-12	SCL-90-R Obsessive-compulsive Behavior	Comparison	1,135		
		Background RH	342	0.92 (0.64,1.31)	0.634
		Low RH	201	0.69 (0.44,1.08)	0.105
		High RH	205	0.97 (0.66,1.44)	0.888
		Low plus High RH	406	0.82 (0.60,1.13)	0.219
12-13	SCL-90-R Paranoid Ideation	Comparison	1,135		
		Background RH	342	0.61 (0.30,1.26)	0.182
		Low RH	201	0.35 (0.12,1.01)	0.052
		High RH	205	0.58 (0.27,1.21)	0.147
		Low plus High RH	406	0.45 (0.23,0.88)	0.019

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
12-14	SCL-90-R Phobic Anxiety	Comparison	1,135		
		Background RH	342	1.14 (0.70,1.85)	0.610
		Low RH	201	0.67 (0.35,1.30)	0.234
		High RH	205	0.66 (0.38,1.15)	0.141
		Low plus High RH	406	0.67 (0.42,1.05)	0.078
12-15	SCL-90-R Psychoticism	Comparison	1,135		
		Background RH	342	0.88 (0.56,1.40)	0.599
		Low RH	201	0.54 (0.29,1.01)	0.055
		High RH	205	1.12 (0.70,1.79)	0.642
		Low plus High RH	406	0.78 (0.52,1.18)	0.242
12-16	SCL-90-R Somatization	Comparison	1,135		
		Background RH	342	0.97 (0.66,1.45)	0.898
		Low RH	201	0.64 (0.38,1.06)	0.081
		High RH	205	1.02 (0.68,1.52)	0.932
		Low plus High RH	406	0.81 (0.57,1.14)	0.223
12-17	SCL-90-R Global Severity Index	Comparison	1,135		
		Background RH	342	0.81 (0.52,1.27)	0.353
		Low RH	201	0.65 (0.37,1.13)	0.123
		High RH	205	0.90 (0.58,1.40)	0.639
		Low plus High RH	406	0.76 (0.52,1.11)	0.160
12-18	SCL-90-R Positive Symptom Total	Comparison	1,135		
		Background RH	342	0.80 (0.52,1.23)	0.299
		Low RH	201	0.49 (0.27,0.89)	0.019
		High RH	205	0.83 (0.52,1.31)	0.413
		Low plus High RH	406	0.64 (0.43,0.94)	0.025
12-19	SCL-90-R Positive Symptom Distress Index	Comparison	1,135		
		Background RH	342	0.81 (0.47,1.40)	0.450
		Low RH	201	0.83 (0.45,1.52)	0.546
		High RH	205	0.84 (0.50,1.41)	0.503
		Low plus High RH	406	0.83 (0.54,1.28)	0.402
13-3	Uncharacterized Hepatitis	Comparison	1,162		
		Background RH	347	1.26 (0.44,3.62)	0.671
		Low RH	209	1.18 (0.33,4.19)	0.796
		High RH	209	2.36 (0.89,6.24)	0.083
		Low plus High RH	418	1.67 (0.70,3.99)	0.249
13-4	Jaundice	Comparison	1,140		
		Background RH	338	1.06 (0.52,2.17)	0.867
		Low RH	206	0.33 (0.08,1.40)	0.133
		High RH	207	0.18 (0.02,1.31)	0.090
		Low plus High RH	413	0.24 (0.07,0.85)	0.027
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	Comparison	1,106		
		Background RH	331	1.37 (0.73,2.58)	0.322
		Low RH	200	0.66 (0.25,1.72)	0.395
		High RH	191	1.16 (0.56,2.44)	0.686
		Low plus High RH	391	0.87 (0.46,1.66)	0.673

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]		p-Value
13-6	Chronic Liver Disease and Cirrhosis (Nonalcohol-related)	Comparison	1,168			
		Background RH	350	1.21	(0.53,2.76)	0.653
		Low RH	210	1.76	(0.79,3.89)	0.164
		High RH	211	1.77	(0.81,3.89)	0.155
		Low plus High RH	421	1.76	(0.95,3.27)	0.071
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	Comparison	1,168			
		Background RH	350	3.05	(0.42,22.37)	0.273
		Low RH	210	3.01	(0.26,34.33)	0.376
		High RH	211	7.06	(0.90,55.13)	0.062
		Low plus High RH	421	4.61	(0.70,30.20)	0.111
13-8	Enlarged Liver	Comparison	1,167			
		Background RH	350	1.03	(0.53,2.00)	0.938
		Low RH	210	0.87	(0.38,1.99)	0.748
		High RH	210	0.87	(0.39,1.94)	0.735
		Low plus High RH	420	0.87	(0.47,1.61)	0.661
13-9	Other Disorders of the Liver	Comparison	1,159			
		Background RH	347	1.06	(0.82,1.36)	0.660
		Low RH	210	1.08	(0.80,1.46)	0.612
		High RH	211	1.16	(0.85,1.58)	0.355
		Low plus High RH	421	1.12	(0.89,1.41)	0.341
13-10	Current Hepatomegaly	Comparison	1,155			
		Background RH	348	1.46	(0.50,4.27)	0.486
		Low RH	209	2.03	(0.70,5.88)	0.189
		High RH	212	0.70	(0.15,3.23)	0.643
		Low plus High RH	421	1.19	(0.43,3.25)	0.741
13-12	AST	Comparison	1,149			
		Background RH	346	1.38	(0.88,2.15)	0.163
		Low RH	207	1.19	(0.68,2.08)	0.535
		High RH	209	1.02	(0.57,1.80)	0.952
		Low plus High RH	416	1.10	(0.72,1.69)	0.659
13-14	ALT	Comparison	1,149			
		Background RH	346	0.76	(0.44,1.29)	0.302
		Low RH	207	1.24	(0.72,2.12)	0.438
		High RH	209	0.79	(0.44,1.43)	0.436
		Low plus High RH	416	0.99	(0.64,1.52)	0.958
13-16	GGT	Comparison	1,149			
		Background RH	346	0.81	(0.52,1.26)	0.352
		Low RH	207	1.38	(0.87,2.19)	0.168
		High RH	209	0.73	(0.43,1.23)	0.240
		Low plus High RH	416	1.00	(0.69,1.45)	0.982
13-18	Alkaline Phosphatase	Comparison	1,150			
		Background RH	347	1.50	(0.93,2.41)	0.094
		Low RH	207	1.26	(0.70,2.27)	0.442
		High RH	211	1.33	(0.78,2.28)	0.298
		Low plus High RH	418	1.30	(0.84,2.00)	0.241

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
13-20	Total Bilirubin	Comparison	1,149		
		Background RH	346	1.05 (0.64,1.74)	0.837
		Low RH	207	1.37 (0.78,2.40)	0.272
		High RH	209	0.70 (0.35,1.42)	0.324
		Low plus High RH	416	0.98 (0.61,1.58)	0.928
13-21	Direct Bilirubin	Comparison	1,149		
		Background RH	346	0.64 (0.13,3.27)	0.592
		Low RH	207	--	--
		High RH	209	--	--
		Low plus High RH	416	--	--
13-23	LDH	Comparison	1,149		
		Background RH	346	1.42 (0.95,2.13)	0.086
		Low RH	207	1.28 (0.80,2.03)	0.301
		High RH	209	0.94 (0.54,1.62)	0.822
		Low plus High RH	416	1.09 (0.74,1.61)	0.647
13-25	Cholesterol	Comparison	1,149		
		Background RH	346	0.90 (0.61,1.32)	0.581
		Low RH	207	0.73 (0.44,1.21)	0.222
		High RH	209	0.63 (0.38,1.02)	0.063
		Low plus High RH	416	0.68 (0.47,0.98)	0.039
13-27	HDL Cholesterol	Comparison	1,149		
		Background RH	346	1.41 (0.99,2.00)	0.055
		Low RH	207	1.15 (0.76,1.75)	0.496
		High RH	209	1.18 (0.80,1.76)	0.407
		Low plus High RH	416	1.17 (0.86,1.59)	0.323
13-29	Cholesterol-HDL Ratio	Comparison	1,149		
		Background RH	346	0.85 (0.64,1.14)	0.280
		Low RH	207	0.98 (0.71,1.37)	0.925
		High RH	209	1.00 (0.72,1.38)	0.998
		Low plus High RH	416	0.99 (0.77,1.27)	0.951
13-31	Triglycerides	Comparison	1,149		
		Background RH	346	0.96 (0.61,1.50)	0.845
		Low RH	207	1.72 (1.11,2.66)	0.015
		High RH	209	1.70 (1.12,2.57)	0.012
		Low plus High RH	416	1.71 (1.23,2.38)	0.001
13-33	Creatine Phosphokinase	Comparison	1,149		
		Background RH	346	1.03 (0.67,1.59)	0.892
		Low RH	207	0.67 (0.38,1.16)	0.151
		High RH	209	0.76 (0.44,1.31)	0.322
		Low plus High RH	416	0.71 (0.47,1.07)	0.105
13-35	Serum Amylase	Comparison	1,149		
		Background RH	346	0.61 (0.28,1.34)	0.216
		Low RH	207	0.93 (0.40,2.16)	0.872
		High RH	209	0.92 (0.37,2.27)	0.848
		Low plus High RH	416	0.92 (0.48,1.79)	0.815

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
13-36	Antibodies for Hepatitis A	Comparison	1,168		
		Background RH	348	0.84 (0.64,1.11)	0.224
		Low RH	209	0.80 (0.58,1.12)	0.192
		High RH	211	0.93 (0.66,1.30)	0.668
		Low plus High RH	420	0.86 (0.67,1.11)	0.254
13-37	Serological Evidence for Prior Hepatitis B Infection	Comparison	1,169		
		Background RH	350	0.44 (0.25,0.77)	0.004
		Low RH	210	0.56 (0.31,0.99)	0.045
		High RH	211	0.63 (0.38,1.06)	0.082
		Low plus High RH	421	0.59 (0.40,0.89)	0.012
13-38	Antibodies for Hepatitis C	Comparison	1,169		
		Background RH	350	0.62 (0.17,2.19)	0.454
		Low RH	210	0.24 (0.03,1.93)	0.180
		High RH	211	0.24 (0.03,1.82)	0.166
		Low plus High RH	421	0.24 (0.05,1.06)	0.059
13-39	Stool Hemoccult	Comparison	1,073		
		Background RH	325	1.68 (0.62,4.58)	0.309
		Low RH	194	1.03 (0.29,3.69)	0.958
		High RH	197	0.90 (0.25,3.28)	0.872
		Low plus High RH	391	0.96 (0.36,2.57)	0.942
13-41	Prealbumin	Comparison	1,149		
		Background RH	346	1.66 (0.68,4.08)	0.268
		Low RH	207	2.11 (0.74,6.02)	0.164
		High RH	209	1.10 (0.30,4.08)	0.881
		Low plus High RH	416	1.52 (0.61,3.80)	0.366
13-43	Albumin	Comparison	1,149		
		Background RH	346	3.06 (0.80,11.70)	0.103
		Low RH	207	--	--
		High RH	209	--	--
		Low plus High RH	416	--	--
13-45	α-1-Acid Glycoprotein	Comparison	1,149		
		Background RH	346	0.95 (0.52,1.73)	0.856
		Low RH	207	1.80 (1.00,3.26)	0.051
		High RH	209	1.15 (0.60,2.21)	0.673
		Low plus High RH	416	1.44 (0.89,2.32)	0.137
13-49	α-2-Macroglobulin	Comparison	1,149		
		Background RH	346	0.87 (0.58,1.29)	0.484
		Low RH	207	0.96 (0.62,1.50)	0.865
		High RH	209	0.89 (0.56,1.42)	0.619
		Low plus High RH	416	0.92 (0.65,1.30)	0.654
13-51	Apolipoprotein B	Comparison	1,149		
		Background RH	346	0.50 (0.17,1.47)	0.207
		Low RH	207	0.65 (0.19,2.19)	0.485
		High RH	209	0.41 (0.09,1.80)	0.238
		Low plus High RH	416	0.51 (0.19,1.40)	0.192

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
13-53	C3 Complement	Comparison	1,149		
		Background RH	346	0.90 (0.38,2.11)	0.805
		Low RH	207	--	--
		High RH	209	0.53 (0.06,4.29)	0.549
		Low plus High RH	416	--	--
13-55	C4 Complement	Comparison	1,149		
		Background RH	346	0.91 (0.58,1.44)	0.698
		Low RH	207	0.52 (0.26,1.06)	0.071
		High RH	209	1.46 (0.85,2.50)	0.169
		Low plus High RH	416	0.87 (0.55,1.40)	0.576
13-57	Haptoglobin	Comparison	1,149		
		Background RH	346	1.21 (0.83,1.77)	0.328
		Low RH	207	1.35 (0.88,2.07)	0.175
		High RH	209	0.87 (0.55,1.39)	0.562
		Low plus High RH	416	1.08 (0.77,1.52)	0.652
13-59	Transferrin	Comparison	1,149		
		Background RH	346	1.30 (0.82,2.07)	0.266
		Low RH	207	0.41 (0.18,0.97)	0.041
		High RH	209	0.62 (0.27,1.40)	0.247
		Low plus High RH	416	0.50 (0.27,0.93)	0.029
13-61	Prothrombin Time	Comparison	892		
		Background RH	268	0.46 (0.05,3.81)	0.468
		Low RH	144	1.47 (0.35,6.15)	0.596
		High RH	156	0.59 (0.06,5.60)	0.644
		Low plus High RH	300	0.91 (0.21,3.97)	0.903
14-3	Acne (Lifetime)	Comparison	1,174		
		Background RH	352	1.21 (0.94,1.56)	0.131
		Low RH	211	1.63 (1.20,2.20)	0.002
		High RH	213	1.30 (0.95,1.76)	0.099
		Low plus High RH	424	1.45 (1.15,1.83)	0.002
14-4	Post-SEA Acne	Comparison	1,173		
		Background RH	352	1.49 (1.10,2.01)	0.009
		Low RH	211	1.68 (1.19,2.37)	0.003
		High RH	213	1.19 (0.84,1.68)	0.332
		Low plus High RH	424	1.41 (1.08,1.83)	0.011
14-5	Post-SEA Acne (No Pre-SEA Acne)	Comparison	787		
		Background RH	227	1.60 (1.01,2.53)	0.046
		Low RH	132	2.19 (1.34,3.58)	0.002
		High RH	140	1.72 (1.07,2.78)	0.026
		Low plus High RH	272	1.93 (1.33,2.82)	<0.001
14-6	Post-SEA Acne (with Pre-SEA Acne)	Comparison	386		
		Background RH	125	1.36 (0.89,2.10)	0.159
		Low RH	79	1.17 (0.70,1.97)	0.549
		High RH	73	0.76 (0.44,1.30)	0.311
		Low plus High RH	152	0.95 (0.64,1.42)	0.800

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
14-8	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (Excluding Participants with Pre-SEA Acne)	Comparison	89		
		Background RH	32	1.08 (0.42,2.79)	0.867
		Low RH	26	0.79 (0.28,2.18)	0.643
		High RH	30	0.98 (0.39,2.47)	0.972
		Low plus High RH	56	0.89 (0.42,1.89)	0.754
14-10	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (All Post-SEA Occurrences)	Comparison	236		
		Background RH	83	1.20 (0.70,2.04)	0.503
		Low RH	57	1.11 (0.61,2.04)	0.729
		High RH	61	0.88 (0.48,1.63)	0.687
		Low plus High RH	118	0.99 (0.62,1.58)	0.955
14-13	Acneiform Lesions	Comparison	1,173		
		Background RH	352	1.72 (1.02,2.90)	0.042
		Low RH	211	0.58 (0.24,1.37)	0.214
		High RH	213	1.08 (0.59,1.95)	0.805
		Low plus High RH	424	0.79 (0.45,1.38)	0.406
14-14	Acneiform Scars	Comparison	1,173		
		Background RH	352	1.43 (0.88,2.32)	0.148
		Low RH	211	0.81 (0.41,1.57)	0.526
		High RH	213	0.77 (0.41,1.46)	0.422
		Low plus High RH	424	0.79 (0.48,1.29)	0.339
14-15	Comedones	Comparison	1,173		
		Background RH	352	0.82 (0.48,1.39)	0.458
		Low RH	211	0.47 (0.22,1.01)	0.052
		High RH	213	0.85 (0.45,1.59)	0.603
		Low plus High RH	424	0.63 (0.38,1.06)	0.084
14-16	Depigmentation	Comparison	1,173		
		Background RH	352	0.42 (0.15,1.21)	0.110
		Low RH	211	1.03 (0.45,2.36)	0.947
		High RH	213	0.68 (0.26,1.80)	0.434
		Low plus High RH	424	0.83 (0.42,1.65)	0.601
14-17	Hyperpigmentation	Comparison	1,173		
		Background RH	352	0.75 (0.44,1.28)	0.295
		Low RH	211	0.95 (0.55,1.63)	0.838
		High RH	213	0.91 (0.52,1.61)	0.747
		Low plus High RH	424	0.93 (0.61,1.41)	0.726
14-18	Inclusion Cysts	Comparison	1,173		
		Background RH	352	1.13 (0.78,1.65)	0.519
		Low RH	211	0.91 (0.57,1.46)	0.704
		High RH	213	1.22 (0.79,1.89)	0.371
		Low plus High RH	424	1.06 (0.75,1.49)	0.756
14-19	Dermatology Index	Comparison	1,173		
		Background RH	352	1.14 (0.85,1.52)	0.387
		Low RH	211	0.72 (0.49,1.04)	0.083
		High RH	213	1.02 (0.73,1.45)	0.890
		Low plus High RH	424	0.86 (0.65,1.13)	0.268

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]		p-Value
15-3	Essential Hypertension	Comparison	1,136			
		Background RH	342	0.88	(0.67,1.16)	0.363
		Low RH	198	0.74	(0.53,1.04)	0.086
		High RH	208	1.32	(0.94,1.87)	0.113
		Low plus High RH	406	1.00	(0.77,1.29)	0.986
15-4	Heart Disease (Excluding Essential Hypertension)	Comparison	1,146			
		Background RH	344	1.33	(0.94,1.89)	0.109
		Low RH	202	1.03	(0.68,1.54)	0.904
		High RH	209	1.21	(0.81,1.82)	0.346
		Low plus High RH	411	1.12	(0.82,1.52)	0.476
15-5	Myocardial Infarction	Comparison	1,146			
		Background RH	344	0.81	(0.53,1.25)	0.345
		Low RH	202	0.60	(0.34,1.04)	0.071
		High RH	209	1.04	(0.63,1.74)	0.872
		Low plus High RH	411	0.79	(0.53,1.19)	0.260
15-6	Stroke or Transient Ischemic Attack	Comparison	1,146			
		Background RH	344	1.21	(0.59,2.45)	0.604
		Low RH	202	1.10	(0.47,2.57)	0.828
		High RH	209	2.16	(0.98,4.77)	0.057
		Low plus High RH	411	1.55	(0.82,2.91)	0.174
15-8	Systolic Blood Pressure	Comparison	1,146			
		Background RH	344	1.06	(0.80,1.42)	0.674
		Low RH	202	0.63	(0.43,0.92)	0.018
		High RH	209	0.82	(0.56,1.19)	0.289
		Low plus High RH	411	0.72	(0.54,0.96)	0.023
15-10	Diastolic Blood Pressure	Comparison	1,146			
		Background RH	344	0.83	(0.44,1.58)	0.577
		Low RH	202	0.96	(0.46,2.02)	0.916
		High RH	209	1.88	(1.04,3.39)	0.036
		Low plus High RH	411	1.35	(0.81,2.24)	0.244
15-11	Heart Sounds	Comparison	1,146			
		Background RH	344	1.08	(0.65,1.80)	0.774
		Low RH	202	1.11	(0.60,2.05)	0.744
		High RH	209	1.38	(0.73,2.59)	0.319
		Low plus High RH	411	1.24	(0.77,1.99)	0.377
15-12	Overall ECG	Comparison	1,146			
		Background RH	344	1.16	(0.88,1.52)	0.298
		Low RH	202	0.86	(0.61,1.20)	0.362
		High RH	209	0.96	(0.67,1.36)	0.802
		Low plus High RH	411	0.91	(0.70,1.17)	0.453
15-13	ECG: RBBB	Comparison	1,146			
		Background RH	344	1.52	(0.84,2.76)	0.169
		Low RH	202	0.56	(0.21,1.46)	0.236
		High RH	209	1.03	(0.45,2.35)	0.951
		Low plus High RH	411	0.76	(0.39,1.49)	0.429

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
15-14	ECG: LBBB	Comparison	1,146		
		Background RH	344	0.92 (0.31,2.74)	0.885
		Low RH	202	0.26 (0.03,2.11)	0.207
		High RH	209	0.69 (0.14,3.41)	0.651
		Low plus High RH	411	0.43 (0.11,1.67)	0.221
15-15	ECG: Nonspecific ST- and T-wave Changes	Comparison	1,128		
		Background RH	337	1.13 (0.83,1.53)	0.448
		Low RH	192	0.79 (0.54,1.16)	0.235
		High RH	206	1.12 (0.77,1.64)	0.544
		Low plus High RH	398	0.95 (0.71,1.27)	0.719
15-16	ECG: Bradycardia	Comparison	1,146		
		Background RH	344	1.65 (1.00,2.74)	0.051
		Low RH	202	1.39 (0.70,2.76)	0.346
		High RH	209	0.88 (0.36,2.16)	0.779
		Low plus High RH	411	1.10 (0.60,2.02)	0.754
15-17	ECG: Tachycardia	Comparison	1,146		
		Background RH	344	1.22 (0.23,6.52)	0.815
		Low RH	202	--	--
		High RH	209	0.52 (0.06,4.54)	0.556
		Low plus High RH	411	--	--
15-18	ECG: Arrhythmia	Comparison	1,146		
		Background RH	344	0.88 (0.58,1.35)	0.563
		Low RH	202	1.03 (0.64,1.67)	0.891
		High RH	209	0.63 (0.34,1.18)	0.150
		Low plus High RH	411	0.80 (0.53,1.22)	0.309
15-19	ECG: Evidence of Prior Myocardial Infarction	Comparison	1,146		
		Background RH	344	0.81 (0.45,1.47)	0.487
		Low RH	202	0.75 (0.37,1.52)	0.422
		High RH	209	0.82 (0.37,1.84)	0.632
		Low plus High RH	411	0.78 (0.44,1.39)	0.406
15-20	Funduscopic Examination	Comparison	1,055		
		Background RH	318	1.44 (0.92,2.26)	0.110
		Low RH	179	1.07 (0.63,1.83)	0.801
		High RH	192	1.23 (0.72,2.08)	0.446
		Low plus High RH	371	1.15 (0.77,1.72)	0.498
15-21	Carotid Bruits	Comparison	1,146		
		Background RH	344	0.95 (0.42,2.12)	0.895
		Low RH	202	0.33 (0.08,1.45)	0.143
		High RH	209	0.77 (0.22,2.76)	0.693
		Low plus High RH	411	0.51 (0.19,1.41)	0.194
15-22	Radial Pulses	Comparison	1,138		
		Background RH	343	1.19 (0.74,1.91)	0.470
		Low RH	201	0.55 (0.26,1.17)	0.120
		High RH	209	0.78 (0.41,1.47)	0.447
		Low plus High RH	410	0.66 (0.39,1.10)	0.112

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
15-23	Femoral Pulses	Comparison	1,128		
		Background RH	337	0.91 (0.21,3.90)	0.897
		Low RH	192	2.69 (0.72,10.01)	0.140
		High RH	206	2.74 (0.59,12.87)	0.200
		Low plus High RH	398	2.72 (0.86,8.62)	0.090
15-24	Popliteal Pulses	Comparison	1,127		
		Background RH	337	0.50 (0.18,1.42)	0.193
		Low RH	191	0.82 (0.29,2.33)	0.712
		High RH	205	1.14 (0.38,3.46)	0.812
		Low plus High RH	396	0.98 (0.43,2.20)	0.952
15-25	Dorsalis Pedis Pulses	Comparison	1,143		
		Background RH	343	0.87 (0.53,1.43)	0.582
		Low RH	201	0.83 (0.46,1.49)	0.522
		High RH	209	1.28 (0.72,2.28)	0.409
		Low plus High RH	410	1.03 (0.66,1.60)	0.893
15-26	Posterior Tibial Pulses	Comparison	1,126		
		Background RH	337	0.48 (0.24,0.96)	0.039
		Low RH	191	0.40 (0.16,0.99)	0.048
		High RH	205	0.99 (0.46,2.12)	0.976
		Low plus High RH	396	0.64 (0.34,1.19)	0.155
15-27	Leg Pulses	Comparison	1,124		
		Background RH	336	0.69 (0.42,1.14)	0.146
		Low RH	190	0.67 (0.37,1.23)	0.198
		High RH	205	1.24 (0.71,2.16)	0.454
		Low plus High RH	395	0.92 (0.60,1.43)	0.719
15-28	Peripheral Pulses	Comparison	1,135		
		Background RH	342	0.91 (0.63,1.30)	0.588
		Low RH	199	0.61 (0.37,0.99)	0.046
		High RH	208	1.17 (0.76,1.80)	0.480
		Low plus High RH	407	0.85 (0.60,1.20)	0.351
15-30	Resting Pressure Index	Comparison	1,112		
		Background RH	336	0.81 (0.39,1.68)	0.565
		Low RH	192	0.65 (0.25,1.65)	0.363
		High RH	203	2.14 (0.96,4.80)	0.064
		Low plus High RH	395	1.20 (0.62,2.32)	0.593
15-32	Hyperemic Pressure Index (1 Minute Post-exercise)	Comparison	1,100		
		Background RH	336	1.05 (0.64,1.71)	0.847
		Low RH	195	0.87 (0.49,1.53)	0.622
		High RH	197	1.16 (0.66,2.05)	0.610
		Low plus High RH	392	1.00 (0.65,1.55)	0.989
15-34	Hyperemic Pressure Index (2 Minutes Post-exercise)	Comparison	1,102		
		Background RH	336	0.85 (0.45,1.61)	0.625
		Low RH	195	0.59 (0.26,1.32)	0.200
		High RH	197	0.86 (0.38,1.92)	0.706
		Low plus High RH	392	0.71 (0.39,1.30)	0.270

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
15-35	Intermittent Claudication and Vascular Insufficiency Index	Comparison	1,146		
		Background RH	344	0.91 (0.42,1.97)	0.806
		Low RH	202	0.38 (0.11,1.27)	0.115
		High RH	209	1.19 (0.52,2.74)	0.681
		Low plus High RH	411	0.68 (0.31,1.46)	0.320
16-13	RBC Morphology	Comparison	1,168		
		Background RH	350	1.02 (0.59,1.76)	0.951
		Low RH	210	1.57 (0.89,2.77)	0.123
		High RH	209	1.93 (1.01,3.70)	0.047
		Low plus High RH	419	1.74 (1.09,2.78)	0.021
16-16	Absolute Neutrophils (Bands) (Zero vs. Nonzero)	Comparison	1,168		
		Background RH	350	0.82 (0.59,1.13)	0.221
		Low RH	210	1.15 (0.80,1.64)	0.456
		High RH	209	0.88 (0.59,1.31)	0.527
		Low plus High RH	419	1.01 (0.76,1.34)	0.971
16-20	Absolute Eosinophils (Zero vs. Nonzero)	Comparison	1,168		
		Background RH	350	0.85 (0.56,1.30)	0.463
		Low RH	210	1.13 (0.71,1.79)	0.605
		High RH	209	0.65 (0.37,1.13)	0.126
		Low plus High RH	419	0.86 (0.58,1.26)	0.425
16-22	Absolute Basophils (Zero vs. Nonzero)	Comparison	1,168		
		Background RH	350	1.04 (0.81,1.32)	0.776
		Low RH	210	1.08 (0.80,1.45)	0.627
		High RH	209	1.06 (0.78,1.44)	0.694
		Low plus High RH	419	1.07 (0.85,1.34)	0.561
16-24	Fibrinogen	Comparison	1,168		
		Background RH	349	1.37 (0.81,2.34)	0.243
		Low RH	210	1.28 (0.71,2.31)	0.402
		High RH	209	0.94 (0.48,1.82)	0.851
		Low plus High RH	419	1.10 (0.68,1.77)	0.700
16-26	Erythrocyte Sedimentation Rate	Comparison	1,168		
		Background RH	350	1.30 (0.86,1.98)	0.216
		Low RH	210	1.25 (0.78,1.98)	0.352
		High RH	209	1.20 (0.74,1.95)	0.457
		Low plus High RH	419	1.22 (0.85,1.76)	0.275
17-3	Occurrence of Kidney Stones	Comparison	1,162		
		Background RH	348	0.98 (0.65,1.47)	0.927
		Low RH	208	1.53 (1.00,2.34)	0.053
		High RH	211	0.87 (0.51,1.48)	0.600
		Low plus High RH	419	1.15 (0.79,1.66)	0.466
17-4	Occurrence of Past Kidney Disease	Comparison	1,153		
		Background RH	346	0.98 (0.75,1.27)	0.882
		Low RH	208	0.83 (0.60,1.14)	0.247
		High RH	209	0.89 (0.64,1.23)	0.475
		Low plus High RH	417	0.86 (0.67,1.09)	0.216

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
17-9	Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero vs. Zero)	Comparison	1,174		
		Background RH	352	1.26 (0.86,1.85)	0.243
		Low RH	211	1.33 (0.87,2.01)	0.188
		High RH	213	0.98 (0.63,1.55)	0.947
		Low plus High RH	424	1.14 (0.82,1.59)	0.436
17-11	Urinary Occult Blood	Comparison	1,174		
		Background RH	352	1.20 (0.54,2.65)	0.654
		Low RH	211	1.92 (0.88,4.20)	0.104
		High RH	213	1.02 (0.34,3.09)	0.968
		Low plus High RH	424	1.40 (0.67,2.91)	0.369
17-12	Urinary WBC Count	Comparison	1,174		
		Background RH	352	1.17 (0.69,1.97)	0.559
		Low RH	211	1.52 (0.88,2.64)	0.134
		High RH	213	1.38 (0.76,2.50)	0.286
		Low plus High RH	424	1.45 (0.93,2.25)	0.098
17-13	Urinary Protein	Comparison	1,174		
		Background RH	352	1.12 (0.56,2.26)	0.748
		Low RH	211	0.64 (0.28,1.48)	0.299
		High RH	213	0.68 (0.31,1.52)	0.351
		Low plus High RH	424	0.66 (0.36,1.22)	0.188
18-3	Past Thyroid Disease	Comparison	1,167		
		Background RH	348	0.94 (0.65,1.37)	0.748
		Low RH	209	0.73 (0.45,1.18)	0.198
		High RH	211	0.69 (0.41,1.14)	0.147
		Low plus High RH	420	0.71 (0.49,1.02)	0.066
18-4	Composite Diabetes Indicator (2002 AFHS Diabetes Definition)	Comparison	1,162		
		Background RH	349	0.74 (0.50,1.10)	0.134
		Low RH	206	1.13 (0.75,1.69)	0.567
		High RH	211	1.25 (0.83,1.88)	0.294
		Low plus High RH	417	1.18 (0.87,1.61)	0.282
18-5	Composite Diabetes Indicator (Pre-2002 AFHS Diabetes Definition)	Comparison	1,162		
		Background RH	349	0.81 (0.56,1.16)	0.247
		Low RH	206	0.97 (0.66,1.44)	0.897
		High RH	211	1.19 (0.80,1.75)	0.390
		Low plus High RH	417	1.08 (0.80,1.45)	0.625
18-8	Time to Diabetes Onset (2002 AFHS Diabetes Definition)	Comparison	1,162		
		Background RH	349	0.69 (0.49,0.96)[b]	0.030[b]
		Low RH	206	1.12 (0.81,1.55)[b]	0.494[b]
		High RH	211	1.09 (0.78,1.50)[b]	0.622[b]
		Low plus High RH	417	1.10 (0.86,1.41)[b]	0.437[b]
18-9	Time to Diabetes Onset (Pre-2002 AFHS Diabetes Definition)	Comparison	1,162		
		Background RH	349	0.71 (0.52,0.97)	0.030
		Low RH	206	1.04 (0.76,1.43)	0.798
		High RH	211	1.02 (0.75,1.39)	0.890
		Low plus High RH	417	1.03 (0.82,1.30)	0.795

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
18-10	Thyroid Gland	Comparison	1,093		
		Background RH	329	0.90 (0.36,2.27)	0.822
		Low RH	201	0.47 (0.11,2.01)	0.306
		High RH	203	--	--
		Low plus High RH	404	--	--
18-11	Testicular Examination	Comparison	1,158		
		Background RH	347	1.00 (0.61,1.63)	0.989
		Low RH	206	0.89 (0.49,1.61)	0.690
		High RH	210	1.53 (0.86,2.70)	0.145
		Low plus High RH	416	1.17 (0.75,1.82)	0.499
18-15	Free T$_4$	Comparison	1,089		
		Background RH	327	0.95 (0.62,1.47)	0.825
		Low RH	201	0.90 (0.54,1.50)	0.695
		High RH	203	0.71 (0.41,1.23)	0.219
		Low plus High RH	404	0.80 (0.54,1.19)	0.270
18-16	Anti-thyroid Antibodies	Comparison	1,089		
		Background RH	327	0.47 (0.06,4.01)	0.492
		Low RH	201	1.71 (0.34,8.68)	0.519
		High RH	203	1.29 (0.14,12.19)	0.827
		Low plus High RH	404	1.48 (0.33,6.68)	0.609
18-18	Fasting Glucose	Comparison	1,162		
		Background RH	349	1.14 (0.81,1.59)	0.455
		Low RH	206	1.25 (0.86,1.82)	0.238
		High RH	211	1.03 (0.70,1.53)	0.869
		Low plus High RH	417	1.14 (0.85,1.52)	0.388
18-20	2-hour Postprandial Glucose (Nondiabetics Only)	Comparison	931		
		Background RH	305	1.06 (0.75,1.49)	0.739
		Low RH	158	1.06 (0.70,1.60)	0.772
		High RH	159	0.78 (0.50,1.22)	0.280
		Low plus High RH	317	0.91 (0.66,1.26)	0.570
18-21	2-hour Postprandial Urinary Glucose (Nondiabetics Only)	Comparison	931		
		Background RH	305	1.35 (1.00,1.82)	0.054
		Low RH	158	0.84 (0.56,1.25)	0.388
		High RH	159	0.82 (0.55,1.22)	0.333
		Low plus High RH	317	0.83 (0.61,1.12)	0.224
18-27	Hemoglobin A1c (Diabetics Only)	Comparison	215		
		Background RH	42	0.68 (0.34,1.36)	0.271
		Low RH	45	1.03 (0.51,2.10)	0.929
		High RH	49	1.33 (0.64,2.77)	0.445
		Low plus High RH	94	1.18 (0.68,2.03)	0.554
18-29	C-peptide (Diabetics Only)	Comparison	215		
		Background RH	42	1.12 (0.45,2.80)	0.807
		Low RH	45	1.63 (0.73,3.65)	0.231
		High RH	49	0.68 (0.30,1.54)	0.356
		Low plus High RH	94	1.03 (0.56,1.92)	0.914

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
18-31	Proinsulin (Diabetics Only)	Comparison	215		
		Background RH	42	1.24 (0.59,2.62)	0.573
		Low RH	45	1.59 (0.75,3.34)	0.225
		High RH	49	1.08 (0.53,2.19)	0.831
		Low plus High RH	94	1.30 (0.75,2.25)	0.351
18-32	GADA (Diabetics Only)	Comparison	215		
		Background RH	42	--	--
		Low RH	45	1.24 (0.24,6.38)	0.794
		High RH	49	0.52 (0.06,4.47)	0.555
		Low plus High RH	94	0.79 (0.19,3.28)	0.749
18-34	Total Testosterone	Comparison	1,161		
		Background RH	348	1.22 (0.85,1.75)	0.279
		Low RH	210	0.97 (0.63,1.47)	0.875
		High RH	210	1.37 (0.91,2.07)	0.135
		Low plus High RH	420	1.15 (0.84,1.58)	0.387
18-36	Free Testosterone	Comparison	1,161		
		Background RH	348	1.24 (0.73,2.11)	0.432
		Low RH	210	0.91 (0.49,1.69)	0.758
		High RH	210	1.19 (0.61,2.31)	0.617
		Low plus High RH	420	1.04 (0.63,1.70)	0.887
18-38	Estradiol	Comparison	1,161		
		Background RH	348	1.70 (0.87,3.32)	0.119
		Low RH	210	0.48 (0.14,1.60)	0.231
		High RH	210	1.08 (0.43,2.71)	0.872
		Low plus High RH	420	0.72 (0.32,1.60)	0.419
18-40	LH	Comparison	1,161		
		Background RH	348	0.84 (0.48,1.48)	0.553
		Low RH	210	0.64 (0.31,1.32)	0.227
		High RH	210	0.67 (0.31,1.48)	0.323
		Low plus High RH	420	0.66 (0.37,1.15)	0.142
18-42	FSH	Comparison	1,161		
		Background RH	348	0.95 (0.56,1.59)	0.835
		Low RH	210	1.03 (0.57,1.86)	0.933
		High RH	210	0.73 (0.32,1.66)	0.449
		Low plus High RH	420	0.86 (0.50,1.48)	0.592
19-14	Lupus Panel: ANA Test	Comparison	1,064		
		Background RH	315	0.92 (0.66,1.29)	0.632
		Low RH	187	0.82 (0.54,1.25)	0.364
		High RH	189	1.33 (0.90,1.97)	0.153
		Low plus High RH	376	1.05 (0.77,1.43)	0.766
19-15	Lupus Panel: Thyroid Microsomal Antibody	Comparison	1,064		
		Background RH	315	1.48 (0.67,3.24)	0.329
		Low RH	187	1.64 (0.65,4.14)	0.298
		High RH	189	1.68 (0.68,4.13)	0.262
		Low plus High RH	376	1.66 (0.82,3.36)	0.162

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
19-16	Lupus Panel: MSK Antismooth Muscle Antibody	Comparison	1,064		
		Background RH	315	3.91 (1.23,12.42)	0.021
		Low RH	187	1.86 (0.47,7.39)	0.376
		High RH	189	--	--
		Low plus High RH	376	--	--
19-17	Lupus Panel: MSK Antimitochondrial Antibody	Comparison	1,064		
		Background RH	315	1.49 (0.13,17.51)	0.750
		Low RH	187	2.48 (0.22,28.05)	0.463
		High RH	189	--	--
		Low plus High RH	376	--	--
19-18	Lupus Panel: MSK Antiparietal Cell Antibody	Comparison	1,064		
		Background RH	315	1.26 (0.57,2.77)	0.568
		Low RH	187	0.62 (0.21,1.81)	0.384
		High RH	189	0.37 (0.11,1.26)	0.112
		Low plus High RH	376	0.48 (0.21,1.12)	0.090
19-19	Lupus Panel: Rheumatoid Factor	Comparison	1,064		
		Background RH	315	1.33 (0.97,1.82)	0.075
		Low RH	187	1.81 (1.28,2.57)	0.001
		High RH	189	0.74 (0.49,1.12)	0.156
		Low plus High RH	376	1.15 (0.86,1.54)	0.336
20-3	Asthma	Comparison	1,165		
		Background RH	348	1.27 (0.80,2.04)	0.311
		Low RH	207	0.87 (0.46,1.64)	0.670
		High RH	211	0.76 (0.39,1.49)	0.427
		Low plus High RH	418	0.81 (0.50,1.33)	0.411
20-4	Bronchitis	Comparison	1,148		
		Background RH	342	1.06 (0.81,1.39)	0.647
		Low RH	203	1.05 (0.76,1.45)	0.773
		High RH	209	1.01 (0.73,1.41)	0.933
		Low plus High RH	412	1.03 (0.80,1.32)	0.808
20-5	Pneumonia	Comparison	1,130		
		Background RH	332	0.90 (0.62,1.31)	0.586
		Low RH	195	1.07 (0.70,1.64)	0.749
		High RH	208	0.79 (0.49,1.27)	0.325
		Low plus High RH	403	0.91 (0.65,1.29)	0.602
20-6	Thorax and Lung Abnormality	Comparison	1,171		
		Background RH	351	1.27 (0.88,1.82)	0.197
		Low RH	211	1.20 (0.79,1.82)	0.395
		High RH	213	1.06 (0.68,1.64)	0.808
		Low plus High RH	424	1.12 (0.81,1.56)	0.479
20-7	X-ray Interpretation	Comparison	1,171		
		Background RH	350	0.83 (0.59,1.17)	0.296
		Low RH	211	0.94 (0.64,1.39)	0.769
		High RH	212	0.69 (0.44,1.09)	0.110
		Low plus High RH	423	0.81 (0.59,1.11)	0.188

Table Ref.	Clinical Parameter	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
20-9	FVC	Comparison	1,159		
		Background RH	348	0.98 (0.62,1.56)	0.946
		Low RH	207	1.10 (0.68,1.77)	0.702
		High RH	212	0.67 (0.38,1.17)	0.160
		Low plus High RH	419	0.85 (0.58,1.27)	0.433
20-11	FEV$_1$	Comparison	1,159		
		Background RH	348	1.04 (0.78,1.38)	0.795
		Low RH	207	1.16 (0.83,1.61)	0.390
		High RH	212	0.95 (0.67,1.36)	0.794
		Low plus High RH	419	1.05 (0.81,1.36)	0.720

[a]Relative risk and confidence interval relative to Comparisons.
[b]Hazard ratio, confidence interval, and p-value, based on proportional hazards model, were given for time to diabetes onset variable.

--: Relative risk, confidence interval, and p-value were not presented because of the sparse number of participants with abnormalities.

Note: RH = Ranch Hand.
   Background: (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
   Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
   High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table G-20. Summary of Adjusted Results for Dichotomous Variables – Model 4 (Ranch Hands: Log$_2$ (1987 Dioxin))

Table Ref.	Clinical Parameter	Adjusted Relative Risk (95% C.I.)[a]	p-Value
9-3	Self-perception of Health	1.06 (0.91,1.22)	0.463
9-4	Appearance of Illness or Distress	1.04 (0.78,1.37)	0.807
9-5	Relative Age Appearance	1.22 (0.99,1.52)	0.061
9-7	Body Mass Index	1.31 (1.17,1.47)	<0.001
10-3	All Skin Neoplasms	1.00 (0.89,1.12)	0.968
10-4	Malignant Skin Neoplasms	1.06 (0.92,1.22)	0.425
10-5	Benign Skin Neoplasms	0.96 (0.86,1.07)	0.469
10-6	Skin Neoplasms of Uncertain Behavior or Unspecified Nature	0.84 (0.50,1.41)	0.509
10-7	Basal Cell Carcinoma	0.99 (0.85,1.15)	0.897
10-8	Squamous Cell Carcinoma	1.16 (0.90,1.50)	0.258
10-9	Nonmelanoma	1.02 (0.88,1.18)	0.789
10-10	Melanoma	1.44 (0.96,2.14)	0.071
10-11	Systemic Neoplasms	1.05 (0.93,1.18)	0.434
10-12	Malignant Systemic Neoplasms	1.00 (0.83,1.21)	0.963
10-13	Benign Systemic Neoplasms	1.03 (0.91,1.16)	0.686
10-14	Systemic Neoplasms of Uncertain Behavior or Unspecified Nature	0.97 (0.65,1.44)	0.880
10-16	Malignant Systemic Neoplasms (Eye, Ear, Face, Head, and Neck)	2.33 (0.74,7.37)	0.146
10-17	Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx)	1.23 (0.64,2.38)	0.541
10-18	Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum)	0.04 (0.00,7.74)	0.009
10-19	Malignant Systemic Neoplasms (Thyroid Gland)	0.85 (0.21,3.39)	0.817
10-20	Malignant Systemic Neoplasms (Bronchus and Lung)	1.21 (0.76,1.93)	0.411
10-21	All Stomach Neoplasms	1.04 (0.56,1.91)	0.910
10-22	Malignant Systemic Neoplasms (Colon and Rectum)	1.60 (0.92,2.78)	0.087
10-23	Malignant Systemic Neoplasms (Urinary System)	0.87 (0.60,1.26)	0.459
10-24	Malignant Systemic Neoplasms (Kidney and Ureter)	0.55 (0.31,0.98)	0.048
10-25	Malignant Systemic Neoplasms (Prostate)	0.92 (0.72,1.18)	0.517
10-26	Malignant Systemic Neoplasms (Penis and Other Male Genital Organs)	3.52 (1.04,11.91)	0.017
10-27	Malignant Systemic Neoplasms (Testicles)	1.39 (0.56,3.45)	0.470
10-28	Malignant Systemic Neoplasms (Bone and Articular Cartilage)	--	--
10-29	Malignant Systemic Neoplasms (Connective and Other Soft Tissues)	2.33 (0.74,7.37)	0.146
10-30	Carcinoma in Situ	1.18 (0.59,2.37)	0.646
10-31	Hodgkin's Disease	0.50 (0.01,16.93)	0.653
10-32	Leukemia	0.40 (0.21,0.74)	0.004
10-33	Other Malignant Systemic Neoplasms (Lymphoid and Histiocytic Tissue)	0.99 (0.53,1.86)	0.985
10-34	Lymphoreticular Sarcoma	1.02 (0.20,5.22)	0.981
10-35	Skin and Systemic Neoplasms	1.03 (0.92,1.16)	0.594
10-36	Malignant Skin and Systemic Neoplasms	1.05 (0.92,1.20)	0.438
10-38	PSA	1.02 (0.76,1.38)	0.874
11-3	Inflammatory Diseases	0.93 (0.58,1.48)	0.750
11-4	Hereditary and Degenerative Diseases	1.00 (0.86,1.16)	0.961
11-5	Peripheral Disorders	1.06 (0.93,1.20)	0.407
11-6	Other Neurological Disorders	1.04 (0.91,1.20)	0.532
11-7	Smell	0.64 (0.45,0.90)	0.010
11-8	Visual Fields	0.67 (0.42,1.09)	0.109
11-9	Light Reaction	1.15 (0.59,2.24)	0.692

Table Ref.	Clinical Parameter	Adjusted Relative Risk (95% C.I.)[a]	p-Value
11-10	Ocular Movement	0.96 (0.48,1.92)	0.912
11-11	Facial Sensation	1.17 (0.57,2.40)	0.677
11-12	Corneal Reflex	1.07 (0.48,2.41)	0.862
11-13	Smile	1.13 (0.63,2.03)	0.681
11-14	Palpebral Fissure	1.00 (0.73,1.39)	0.981
11-15	Balance	1.44 (0.90,2.32)	0.124
11-16	Gag Reflex	1.37 (0.69,2.70)	0.376
11-17	Speech	0.89 (0.54,1.49)	0.662
11-18	Tongue Position Relative to Midline	2.56 (0.85,7.68)	0.069
11-19	Shoulder Shrug	0.81 (0.35,1.86)	0.622
11-20	Cranial Nerve Index	0.95 (0.79,1.14)	0.611
11-21	Pinprick	1.06 (0.86,1.30)	0.584
11-22	Light Touch	1.11 (0.86,1.43)	0.414
11-23	Muscle Status	0.96 (0.76,1.20)	0.701
11-27	Babinski Reflex	0.79 (0.52,1.20)	0.277
11-28	Any Symmetric Peripheral Abnormality	1.03 (0.90,1.18)	0.675
11-29	Possible Peripheral Neuropathy	1.01 (0.88,1.17)	0.851
11-30	Probable Peripheral Neuropathy	0.96 (0.75,1.22)	0.725
11-31	Tremor	1.03 (0.83,1.27)	0.798
11-32	Coordination	1.06 (0.79,1.41)	0.719
11-33	Romberg Sign	1.44 (0.90,2.32)	0.124
11-34	Gait	0.97 (0.79,1.20)	0.798
11-35	CNS Index	0.98 (0.84,1.15)	0.830
12-3	Psychoses	0.97 (0.80,1.17)	0.732
12-4	Alcohol Dependence	0.87 (0.72,1.06)	0.180
12-5	Drug Dependence	0.51 (0.16,1.61)	0.224
12-6	Anxiety	0.97 (0.87,1.08)	0.547
12-7	Other Neuroses	1.01 (0.90,1.14)	0.819
12-8	SCL-90-R Anxiety	0.94 (0.79,1.11)	0.443
12-9	SCL-90-R Depression	0.97 (0.84,1.14)	0.744
12-10	SCL-90-R Hostility	0.94 (0.77,1.15)	0.548
12-11	SCL-90-R Interpersonal Sensitivity	0.92 (0.77,1.10)	0.350
12-12	SCL-90-R Obsessive-compulsive Behavior	0.99 (0.86,1.13)	0.877
12-13	SCL-90-R Paranoid Ideation	0.94 (0.72,1.22)	0.649
12-14	SCL-90-R Phobic Anxiety	0.80 (0.66,0.96)	0.014
12-15	SCL-90-R Psychoticism	1.03 (0.87,1.23)	0.700
12-16	SCL-90-R Somatization	1.01 (0.88,1.17)	0.862
12-17	SCL-90-R Global Severity	0.97 (0.83,1.13)	0.672
12-18	SCL-90-R Positive Symptom Total	0.92 (0.79,1.09)	0.341
12-19	SCL-90-R Positive Symptom Distress Index	1.07 (0.89,1.28)	0.497
13-3	Uncharacterized Hepatitis	1.02 (0.71,1.45)	0.931
13-4	Jaundice	0.59 (0.39,0.90)	0.014
13-5	Chronic Liver Disease and Cirrhosis (Alcohol-related)	1.08 (0.83,1.41)	0.577
13-6	Chronic Liver Disease and Cirrhosis (Nonalcohol-related)	1.02 (0.76,1.38)	0.883
13-7	Liver Abscess and Sequelae of Chronic Liver Disease	1.14 (0.63,2.06)	0.679
13-8	Enlarged Liver	0.91 (0.69,1.21)	0.513
13-9	Other Disorders of the Liver	1.02 (0.91,1.13)	0.756
13-10	Current Hepatomegaly	0.94 (0.64,1.36)	0.733
13-12	AST	1.06 (0.87,1.29)	0.574

Table Ref.	Clinical Parameter	Adjusted Relative Risk (95% C.I.)[a]	p-Value
13-14	ALT	1.12 (0.90,1.40)	0.313
13-16	GGT	1.02 (0.85,1.22)	0.850
13-18	Alkaline Phosphatase	0.92 (0.77,1.10)	0.356
13-20	Total Bilirubin	0.98 (0.79,1.23)	0.883
13-21	Direct Bilirubin	0.53 (0.20,1.40)	0.191
13-23	LDH	0.90 (0.76,1.08)	0.257
13-25	Cholesterol	0.94 (0.80,1.10)	0.435
13-27	HDL Cholesterol	0.93 (0.81,1.07)	0.334
13-29	Cholesterol-HDL Ratio	0.99 (0.88,1.11)	0.866
13-31	Triglycerides	1.20 (1.03,1.40)	0.020
13-33	Creatine Phosphokinase	0.90 (0.75,1.09)	0.280
13-35	Serum Amylase	0.88 (0.66,1.19)	0.404
13-36	Antibodies for Hepatitis A	1.06 (0.94,1.19)	0.354
13-37	Serological Evidence of Prior Hepatitis B Infection	1.15 (0.94,1.40)	0.184
13-38	Antibodies for Hepatitis C	0.62 (0.36,1.09)	0.099
13-39	Stool Hemoccult	1.26 (0.78,2.04)	0.328
13-41	Prealbumin	0.99 (0.68,1.43)	0.942
13-43	Albumin	0.37 (0.15,0.94)	0.030
13-45	α-1-Acid Glycoprotein	0.93 (0.75,1.15)	0.505
13-49	α-2-Macroglobulin	1.04 (0.88,1.23)	0.661
13-51	Apolipoprotein B	1.22 (0.74,2.00)	0.439
13-53	C3 Complement	0.76 (0.46,1.24)	0.265
13-55	C4 Complement	1.20 (0.96,1.49)	0.097
13-57	Haptoglobin	0.89 (0.76,1.03)	0.111
13-59	Transferrin	0.83 (0.65,1.05)	0.120
13-61	Prothrombin Time	0.65 (0.30,1.41)	0.294
14-3	Acne (Lifetime)	0.95 (0.86,1.05)	0.332
14-4	Post-SEA Acne	0.92 (0.82,1.03)	0.161
14-5	Post-SEA Acne (No Pre-SEA Acne)	0.98 (0.84,1.14)	0.763
14-6	Post-SEA Acne (with Pre-SEA Acne)	0.89 (0.74,1.07)	0.222
14-8	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (Excluding Participants with Pre-SEA Acne)	1.03 (0.78,1.37)	0.836
14-10	Location of Post-SEA Acne — Temples, Eyes, or Ears vs. Other Sites (All Post-SEA Occurrences)	1.00 (0.83,1.21)	0.962
14-13	Acneiform Lesions	0.86 (0.71,1.06)	0.155
14-14	Acneiform Scars	0.87 (0.71,1.06)	0.166
14-15	Comedones	0.87 (0.71,1.08)	0.222
14-16	Depigmentation	1.35 (0.92,1.97)	0.116
14-17	Hyperpigmentation	0.96 (0.79,1.17)	0.696
14-18	Inclusion Cysts	1.03 (0.89,1.20)	0.660
14-19	Dermatology Index	0.97 (0.86,1.09)	0.578
15-3	Essential Hypertension	1.11 (0.98,1.25)	0.088
15-4	Heart Disease (Excluding Essential Hypertension)	0.90 (0.78,1.06)	0.200
15-5	Myocardial Infarction	1.03 (0.85,1.24)	0.778
15-6	Stroke or Transient Ischemic Attack	1.04 (0.76,1.44)	0.802
15-8	Systolic Blood Pressure	0.86 (0.75,0.98)	0.023
15-10	Diastolic Blood Pressure	1.14 (0.89,1.46)	0.306
15-11	Heart Sounds	1.07 (0.86,1.34)	0.526
15-12	Overall ECG	0.96 (0.85,1.08)	0.471

Table Ref.	Clinical Parameter	Adjusted Relative Risk (95% C.I.)[a]	p-Value
15-13	ECG: RBBB	0.95 (0.71,1.27)	0.709
15-14	ECG: LBBB	0.84 (0.50,1.44)	0.538
15-15	ECG: Nonspecific ST- and T-wave Changes	0.95 (0.83,1.09)	0.486
15-16	ECG: Bradycardia	0.84 (0.65,1.09)	0.202
15-17	ECG: Tachycardia	0.79 (0.36,1.76)	0.570
15-18	ECG: Arrhythmia	0.89 (0.73,1.08)	0.230
15-19	ECG: Evidence of Prior Myocardial Infarction	1.20 (0.88,1.64)	0.252
15-20	Funduscopic Examination	1.03 (0.85,1.24)	0.774
15-21	Carotid Bruits	0.74 (0.48,1.15)	0.186
15-22	Radial Pulses	1.03 (0.81,1.30)	0.828
15-23	Femoral Pulses	0.94 (0.58,1.52)	0.797
15-24	Popliteal Pulses	0.99 (0.66,1.48)	0.954
15-25	Dorsalis Pedis Pulses	1.05 (0.85,1.29)	0.646
15-26	Posterior Tibial Pulses	1.13 (0.84,1.52)	0.403
15-27	Leg Pulses	1.06 (0.87,1.30)	0.561
15-28	Peripheral Pulses	1.10 (0.93,1.29)	0.265
15-30	Resting Pressure Index	0.96 (0.70,1.32)	0.820
15-32	Hyperemic Pressure Index (1 Minute Post-exercise)	1.08 (0.87,1.33)	0.488
15-34	Hyperemic Pressure Index (2 Minutes Post-exercise)	0.95 (0.70,1.29)	0.757
15-35	Intermittent Claudication and Vascular Insufficiency Index	1.02 (0.72,1.45)	0.899
16-13	RBC Morphology	1.06 (0.85,1.32)	0.597
16-16	Absolute Neutrophils (Bands) (Zero vs. Nonzero)	1.05 (0.92,1.20)	0.496
16-20	Absolute Eosinophils (Zero vs. Nonzero)	0.93 (0.78,1.12)	0.447
16-22	Absolute Basophils (Zero vs. Nonzero)	0.95 (0.85,1.05)	0.300
16-24	Fibrinogen	0.98 (0.79,1.22)	0.855
16-26	Erythrocyte Sedimentation Rate	1.04 (0.87,1.23)	0.679
17-3	Occurrence of Kidney Stones	0.99 (0.83,1.17)	0.877
17-4	Occurrence of Past Kidney Disease	1.02 (0.91,1.14)	0.734
17-9	Urinary Microalbumin to Urinary Creatinine Ratio (Nonzero vs. Zero)	0.94 (0.81,1.09)	0.410
17-11	Urinary Occult Blood	1.04 (0.74,1.46)	0.834
17-12	Urinary WBC Count	0.97 (0.80,1.17)	0.735
17-13	Urinary Protein	0.98 (0.74,1.29)	0.863
18-3	Past Thyroid Disease	0.98 (0.83,1.16)	0.828
18-4	Composite Diabetes Indicator (2002 AFHS Diabetes Definition)	1.29 (1.10,1.51)	0.001
18-5	Composite Diabetes Indicator (Pre-2002 AFHS Diabetes Definition)	1.27 (1.09,1.47)	0.001
18-8	Time to Diabetes Onset (2002 AFHS Diabetes Definition)	1.28 (1.12,1.46)[b]	<0.001[b]
18-9	Time to Diabetes Onset (Pre-2002 AFHS Diabetes Definition)	1.26 (1.12,1.43)[b]	<0.001[b]
18-10	Thyroid Gland	0.73 (0.47,1.13)	0.162
18-11	Testicular Examination	1.11 (0.90,1.36)	0.344
18-15	Free T$_4$	0.94 (0.78,1.13)	0.511
18-16	Anti-thyroid Antibodies	1.02 (0.54,1.94)	0.953
18-18	Fasting Glucose	1.02 (0.89,1.18)	0.729
18-20	2-hour Postprandial Glucose (Nondiabetics Only)	0.88 (0.75,1.02)	0.091
18-21	2-hour Postprandial Urinary Glucose (Nondiabetics Only)	0.87 (0.76,0.99)	0.040
18-27	Hemoglobin A1c (Diabetics Only)	1.35 (1.01,1.80)	0.031
18-29	C-peptide (Diabetics Only)	0.85 (0.62,1.17)	0.324
18-31	Proinsulin (Diabetics Only)	0.92 (0.71,1.19)	0.536
18-32	GADA (Diabetics Only)	1.65 (0.78,3.49)	0.162
18-34	Total Testosterone	1.02 (0.88,1.19)	0.800

Table Ref.	Clinical Parameter	Adjusted Relative Risk (95% C.I.)[a]	p-Value
18-36	Free Testosterone	1.25 (0.96,1.62)	0.093
18-38	Estradiol	0.97 (0.71,1.33)	0.847
18-40	LH	0.92 (0.70,1.20)	0.524
18-42	FSH	1.05 (0.80,1.38)	0.700
19-14	Lupus Panel: ANA Test	1.15 (0.99,1.33)	0.058
19-15	Lupus Panel: Thyroid Microsomal Antibody	1.01 (0.75,1.37)	0.944
19-16	Lupus Panel: MSK Antismooth Muscle Antibody	0.47 (0.26,0.85)	0.013
19-17	Lupus Panel: MSK Antimitochondrial Antibody	0.45 (0.19,1.05)	0.084
19-18	Lupus Panel: MSK Antiparietal Cell Antibody	0.80 (0.54,1.19)	0.280
19-19	Lupus Panel: Rheumatoid Factor	0.87 (0.77,1.00)	0.042
20-3	Asthma	0.88 (0.71,1.08)	0.225
20-4	Bronchitis	0.99 (0.88,1.11)	0.851
20-5	Pneumonia	0.94 (0.79,1.10)	0.433
20-6	Thorax and Lung Abnormality	0.93 (0.80,1.07)	0.315
20-7	X-ray Interpretation	0.91 (0.78,1.05)	0.184
20-9	FVC	0.93 (0.77,1.12)	0.452
20-11	FEV$_1$	1.03 (0.91,1.16)	0.677

[a]Relative risk for a twofold increase in 1987 dioxin.
[b]Hazard ratio, confidence interval, and p-value, based on proportional hazards model, were given for time to
 diabetes onset variable.

--: Relative risk, confidence interval, and p-value were not presented because of the sparse number of Ranch Hands
    with abnormalities.

Table G-21. Summary of Adjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
11-24	Patellar Reflex	Active or Very Active vs. Sluggish or Absent	All	0.94 (0.76,1.18)	0.608
			Officer	0.83 (0.59,1.17)	0.283
			Enlisted Flyer	0.85 (0.50,1.44)	0.543
			Enlisted Groundcrew	1.12 (0.80,1.56)	0.512
		Sluggish, Active, or Very Active vs. Absent	All	1.48 (0.89,2.44)	0.130
			Officer	1.48 (0.70,3.13)	0.307
			Enlisted Flyer	1.11 (0.28,4.30)	0.885
			Enlisted Groundcrew	1.61 (0.75,3.45)	0.217
11-25	Achilles Reflex	Active or Very Active vs. Sluggish or Absent	All	1.10 (0.90,1.34)	0.357
			Officer	1.42 (1.03,1.95)	0.031
			Enlisted Flyer	0.89 (0.55,1.46)	0.646
			Enlisted Groundcrew	0.95 (0.70,1.27)	0.709
		Sluggish, Active, or Very Active vs. Absent	All	1.13 (0.89,1.43)	0.321
			Officer	1.14 (0.79,1.63)	0.478
			Enlisted Flyer	1.03 (0.60,1.76)	0.928
			Enlisted Groundcrew	1.17 (0.80,1.70)	0.422
11-26	Biceps Reflex	Active or Very Active vs. Sluggish or Absent	All	1.02 (0.82,1.25)	0.877
			Officer	0.97 (0.70,1.34)	0.842
			Enlisted Flyer	0.73 (0.44,1.21)	0.220
			Enlisted Groundcrew	1.21 (0.89,1.66)	0.228
		Sluggish, Active, or Very Active vs. Absent	All	1.08 (0.57,2.04)	0.825
			Officer	0.38 (0.10,1.41)	0.148
			Enlisted Flyer	1.24 (0.38,4.05)	0.724
			Enlisted Groundcrew	2.11 (0.76,5.81)	0.150

Table G-21. Summary of Adjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
13-47	α-1-Antitrypsin	Abnormal Low vs. Normal	All	0.61 (0.27,1.40)	0.242
			Officer	0.94 (0.34,2.62)	0.902
			Enlisted Flyer	--	--
			Enlisted Groundcrew	0.33 (0.07,1.55)	0.160
		Abnormal High vs. Normal	All	1.16 (0.86,1.58)	0.324
			Officer	1.00 (0.57,1.74)	0.992
			Enlisted Flyer	1.28 (0.67,2.45)	0.458
			Enlisted Groundcrew	1.23 (0.79,1.90)	0.361
16-4	RBC Count	Abnormal Low vs. Normal	All	1.00 (0.70,1.43)	0.995
			Officer	1.14 (0.70,1.86)	0.608
			Enlisted Flyer	0.90 (0.37,2.21)	0.823
			Enlisted Groundcrew	0.85 (0.44,1.64)	0.627
		Abnormal High vs. Normal	All	0.85 (0.46,1.57)	0.599
			Officer	1.50 (0.43,5.25)	0.522
			Enlisted Flyer	0.48 (0.12,1.84)	0.282
			Enlisted Groundcrew	0.84 (0.36,1.94)	0.676
16-6	WBC Count	Abnormal Low vs. Normal	All	0.89 (0.65,1.21)	0.463
			Officer	0.79 (0.50,1.27)	0.330
			Enlisted Flyer	1.34 (0.68,2.66)	0.395
			Enlisted Groundcrew	0.82 (0.48,1.38)	0.446
		Abnormal High vs. Normal	All	0.84 (0.44,1.60)	0.598
			Officer	0.62 (0.16,2.42)	0.490
			Enlisted Flyer	1.50 (0.44,5.13)	0.518
			Enlisted Groundcrew	0.72 (0.28,1.81)	0.483
16-8	Hemoglobin	Abnormal Low vs. Normal	All	1.00 (0.75,1.34)	0.989
			Officer	0.93 (0.60,1.43)	0.731
			Enlisted Flyer	1.34 (0.66,2.72)	0.415
			Enlisted Groundcrew	0.97 (0.60,1.56)	0.898
		Abnormal High vs. Normal	All	0.39 (0.11,1.41)	0.151
			Officer	1.46 (0.10,20.48)	0.778
			Enlisted Flyer	2.63 (0.48,14.32)	0.264
			Enlisted Groundcrew	--	--

Table G-21. Summary of Adjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons)
(Continued)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
16-10	Hematocrit	Abnormal Low vs. Normal	All	0.88 (0.57,1.36)	0.561
			Officer	0.95 (0.52,1.76)	0.880
			Enlisted Flyer	0.90 (0.28,2.82)	0.850
			Enlisted Groundcrew	0.78 (0.37,1.63)	0.507
	Hematocrit (continued)	Abnormal High vs. Normal	All	0.83 (0.30,2.34)	0.731
			Officer	2.93 (0.26,32.53)	0.381
			Enlisted Flyer	1.23 (0.17,8.94)	0.836
			Enlisted Groundcrew	0.40 (0.08,2.00)	0.264
16-12	Platelet Count	Abnormal Low vs. Normal	All	0.81 (0.40,1.65)	0.559
			Officer	2.29 (0.81,6.52)	0.119
			Enlisted Flyer	0.27 (0.03,2.32)	0.232
			Enlisted Groundcrew	0.27 (0.06,1.24)	0.093
		Abnormal High vs. Normal	All	0.53 (0.19,1.50)	0.231
			Officer	0.77 (0.07,8.58)	0.835
			Enlisted Flyer	1.23 (0.08,20.09)	0.883
			Enlisted Groundcrew	0.41 (0.11,1.49)	0.175
18-6	Diabetic Control (2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	All	0.87 (0.51,1.46)	0.591
			Officer	1.15 (0.48,2.73)	0.751
			Enlisted Flyer	1.34 (0.41,4.35)	0.630
			Enlisted Groundcrew	0.56 (0.24,1.29)	0.174
		Diet and Exercise vs. Nondiabetic	All	0.86 (0.49,1.51)	0.596
			Officer	0.70 (0.28,1.77)	0.449
			Enlisted Flyer	1.83 (0.56,5.99)	0.317
			Enlisted Groundcrew	0.65 (0.25,1.71)	0.381
		Oral Hypoglycemics vs. Nondiabetic	All	0.93 (0.67,1.29)	0.665
			Officer	0.84 (0.48,1.46)	0.535
			Enlisted Flyer	0.68 (0.31,1.47)	0.325
			Enlisted Groundcrew	1.14 (0.71,1.83)	0.595
		Requiring Insulin vs. Nondiabetic	All	1.09 (0.60,1.97)	0.775
			Officer	1.03 (0.40,2.62)	0.952
			Enlisted Flyer	0.58 (0.11,3.08)	0.520
			Enlisted Groundcrew	1.40 (0.58,3.37)	0.458

Table G-21. Summary of Adjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
18-7	Diabetic Control (Pre-2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	All	0.83 (0.56,1.24)	0.361
			Officer	1.63 (0.84,3.19)	0.149
			Enlisted Flyer	0.71 (0.28,1.80)	0.477
			Enlisted Groundcrew	0.51 (0.27,0.96)	0.037
	Diabetic Control (Pre-2002 AFHS Diabetes Definition) (continued)	Diet and Exercise vs. Nondiabetic	All	0.89 (0.51,1.56)	0.690
			Officer	0.82 (0.34,2.01)	0.672
			Enlisted Flyer	1.74 (0.53,5.71)	0.360
			Enlisted Groundcrew	0.63 (0.24,1.66)	0.350
		Oral Hypoglycemics vs. Nondiabetic	All	0.92 (0.67,1.28)	0.626
			Officer	0.88 (0.51,1.53)	0.645
			Enlisted Flyer	0.64 (0.30,1.39)	0.260
			Enlisted Groundcrew	1.09 (0.68,1.76)	0.713
		Requiring Insulin vs. Nondiabetic	All	1.08 (0.60,1.96)	0.797
			Officer	1.07 (0.42,2.73)	0.886
			Enlisted Flyer	0.55 (0.10,2.92)	0.480
			Enlisted Groundcrew	1.35 (0.56,3.26)	0.507
18-13	TSH	Abnormal Low vs. Normal	All	0.21 (0.03,1.71)	0.144
			Officer	--	--
			Enlisted Flyer	1.34 (0.10,17.22)	0.822
			Enlisted Groundcrew	--	--
		Abnormal High vs. Normal	All	1.49 (0.82,2.72)	0.190
			Officer	1.34 (0.56,3.20)	0.512
			Enlisted Flyer	1.38 (0.27,6.96)	0.696
			Enlisted Groundcrew	1.75 (0.67,4.59)	0.253
18-23	Fasting Insulin	Abnormal Low vs. Normal	All	0.77 (0.54,1.08)	0.127
			Officer	1.01 (0.62,1.64)	0.970
			Enlisted Flyer	0.56 (0.22,1.45)	0.234
			Enlisted Groundcrew	0.60 (0.34,1.06)	0.077
		Abnormal High vs. Normal	All	1.43 (0.97,2.10)	0.072
			Officer	1.64 (0.82,3.28)	0.163
			Enlisted Flyer	0.61 (0.21,1.72)	0.349
			Enlisted Groundcrew	1.67 (0.98,2.83)	0.059

Table G-21. Summary of Adjusted Results for Polytomous Variables – Model 1 (Ranch Hands vs. Comparisons) (Continued)

Table Ref.	Clinical Parameter	Contrast	Occupational Category	Adjusted Relative Risk (95% C.I.)	p-Value
18-25	2-hour Postprandial Insulin (Nondiabetics Only)	Abnormal Low vs. Normal	All	1.27 (0.79,2.04)	0.324
			Officer	1.28 (0.64,2.57)	0.480
			Enlisted Flyer	0.92 (0.19,4.38)	0.912
			Enlisted Groundcrew	1.33 (0.65,2.71)	0.438
		Abnormal High vs. Normal	All	0.93 (0.74,1.16)	0.533
			Officer	1.19 (0.84,1.69)	0.336
			Enlisted Flyer	1.07 (0.61,1.89)	0.806
			Enlisted Groundcrew	0.70 (0.50,0.99)	0.043
20-13	Loss of Vital Capacity	Mild vs. None	All	0.72 (0.48,1.09)	0.125
			Officer	0.77 (0.35,1.69)	0.514
			Enlisted Flyer	0.68 (0.29,1.61)	0.379
			Enlisted Groundcrew	0.72 (0.40,1.29)	0.264
		Moderate or Severe vs. None	All	0.84 (0.42,1.66)	0.612
			Officer	1.14 (0.39,3.40)	0.809
			Enlisted Flyer	0.25 (0.03,2.20)	0.211
			Enlisted Groundcrew	0.92 (0.34,2.49)	0.866
20-14	Obstructive Abnormality	Mild vs. None	All	1.03 (0.84,1.27)	0.748
			Officer	1.17 (0.86,1.60)	0.324
			Enlisted Flyer	0.59 (0.35,0.99)	0.046
			Enlisted Groundcrew	1.15 (0.83,1.59)	0.413
		Moderate vs. None	All	0.86 (0.60,1.25)	0.436
			Officer	1.34 (0.72,2.50)	0.362
			Enlisted Flyer	0.63 (0.29,1.37)	0.246
			Enlisted Groundcrew	0.65 (0.36,1.18)	0.158
		Severe vs. None	All	1.03 (0.58,1.84)	0.915
			Officer	1.70 (0.68,4.23)	0.252
			Enlisted Flyer	0.71 (0.21,2.37)	0.577
			Enlisted Groundcrew	0.70 (0.26,1.83)	0.463

--: Relative risk, confidence interval, and p-value were not presented because of the sparse number of participants with abnormalities.

Table G-22. Summary of Adjusted Results for Polytomous Variables – Model 2 (Ranch Hands: Log$_2$ (Initial Dioxin))

Table Ref.	Clinical Parameter	Contrast	Adjusted Relative Risk (95% C.I.)[a]	p-Value
11-24	Patellar Reflex	Active or Very Active vs. Sluggish or Absent	1.02 (0.83,1.25)	0.873
		Sluggish, Active, or Very Active vs. Absent	1.37 (0.95,1.99)	0.093
11-25	Achilles Reflex	Active or Very Active vs. Sluggish or Absent	1.05 (0.86,1.28)	0.656
		Sluggish, Active, or Very Active vs. Absent	1.04 (0.84,1.30)	0.704
11-26	Biceps Reflex	Active or Very Active vs. Sluggish or Absent	0.92 (0.75,1.12)	0.410
		Sluggish, Active, or Very Active vs. Absent	1.40 (0.85,2.30)	0.181
13-47	α-1-Antitrypsin	Abnormal Low vs. Normal	0.54 (0.14,2.09)	0.374
		Abnormal High vs. Normal	0.93 (0.74,1.17)	0.527
16-4	RBC Count	Abnormal Low vs. Normal	1.11 (0.81,1.54)	0.511
		Abnormal High vs. Normal	1.12 (0.67,1.88)	0.659
16-6	WBC Count	Abnormal Low vs. Normal	1.08 (0.82,1.43)	0.576
		Abnormal High vs. Normal	1.04 (0.49,2.21)	0.908
16-8	Hemoglobin	Abnormal Low vs. Normal	1.10 (0.86,1.40)	0.448
		Abnormal High vs. Normal	0.42 (0.03,6.68)	0.542
16-10	Hematocrit	Abnormal Low vs. Normal	1.38 (0.95,2.00)	0.089
		Abnormal High vs. Normal	1.51 (0.70,3.25)	0.290
16-12	Platelet Count	Abnormal Low vs. Normal	0.73 (0.32,1.64)	0.441
		Abnormal High vs. Normal	1.08 (0.32,3.61)	0.897
18-6	Diabetic Control (2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	0.77 (0.48,1.23)	0.279
		Diet and Exercise vs. Nondiabetic	0.88 (0.48,1.62)	0.688
		Oral Hypoglycemics vs. Nondiabetic	1.21 (0.91,1.62)	0.195
		Requiring Insulin vs. Nondiabetic	2.78 (1.61,4.82)	<0.001
18-7	Diabetic Control (Pre-2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	1.09 (0.75,1.58)	0.644
		Diet and Exercise vs. Nondiabetic	0.91 (0.50,1.67)	0.768
		Oral Hypoglycemics vs. Nondiabetic	1.27 (0.95,1.70)	0.104
		Requiring Insulin vs. Nondiabetic	2.90 (1.68,5.01)	<0.001
18-13	TSH	Abnormal Low vs. Normal	1.85 (0.48,7.20)	0.374
		Abnormal High vs. Normal	1.00 (0.60,1.66)	0.989
18-23	Fasting Insulin	Abnormal Low vs. Normal	0.77 (0.49,1.20)	0.246
		Abnormal High vs. Normal	1.54 (1.13,2.09)	0.006
18-25	2-hour Postprandial Insulin (Nondiabetics Only)	Abnormal Low vs. Normal	1.12 (0.68,1.84)	0.661
		Abnormal High vs. Normal	1.18 (0.96,1.46)	0.116
20-13	Loss of Vital Capacity	Mild vs. None	0.84 (0.60,1.17)	0.298
		Moderate or Severe vs. None	0.86 (0.43,1.70)	0.661
20-14	Obstructive Abnormality	Mild vs. None	0.93 (0.77,1.13)	0.470
		Moderate vs. None	0.64 (0.43,0.94)	0.023
		Severe vs. None	0.44 (0.20,0.95)	0.036

[a]Relative risk for a twofold increase in initial dioxin.

Table G-23. Summary of Adjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
11-24	Patellar Reflex	Active or Very Active vs. Sluggish or Absent	Comparison	1,160		
			Background RH	348	0.81 (0.59,1.09)	0.165
			Low RH	209	1.10 (0.79,1.55)	0.564
			High RH	208	1.02 (0.71,1.47)	0.895
			Low plus High RH	417	1.06 (0.82,1.39)	0.648
		Sluggish, Active, or Very Active vs. Absent	Comparison	1,160		
			Background RH	348	0.94 (0.43,2.03)	0.866
			Low RH	209	1.69 (0.84,3.41)	0.140
			High RH	208	2.11 (1.01,4.43)	0.048
			Low plus High RH	417	1.89 (1.07,3.33)	0.027
11-25	Achilles Reflex	Active or Very Active vs. Sluggish or Absent	Comparison	1,160		
			Background RH	349	1.13 (0.87,1.47)	0.370
			Low RH	210	1.13 (0.82,1.57)	0.463
			High RH	208	1.05 (0.75,1.46)	0.794
			Low plus High RH	418	1.09 (0.85,1.40)	0.511
		Sluggish, Active, or Very Active vs. Absent	Comparison	1,160		
			Background RH	349	1.04 (0.75,1.44)	0.810
			Low RH	210	1.29 (0.90,1.85)	0.167
			High RH	208	1.15 (0.77,1.72)	0.490
			Low plus High RH	418	1.22 (0.91,1.63)	0.181
11-26	Biceps Reflex	Active or Very Active vs. Sluggish or Absent	Comparison	1,163		
			Background RH	350	0.88 (0.66,1.18)	0.397
			Low RH	210	1.29 (0.94,1.78)	0.118
			High RH	208	0.99 (0.70,1.40)	0.944
			Low plus High RH	418	1.13 (0.88,1.46)	0.345
		Sluggish, Active, or Very Active vs. Absent	Comparison	1,163		
			Background RH	350	0.75 (0.27,2.04)	0.569
			Low RH	210	0.97 (0.35,2.64)	0.947
			High RH	208	1.67 (0.69,4.04)	0.258
			Low plus High RH	418	1.27 (0.61,2.64)	0.526

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
13-47	α-1-Antitrypsin	Abnormal Low vs. Normal	Comparison	1,149		
			Background RH	346	0.81 (0.32,2.07)	0.659
			Low RH	207	0.33 (0.04,2.49)	0.282
			High RH	209	0.35 (0.04,2.77)	0.321
			Low plus High RH	416	0.34 (0.08,1.50)	0.154
		Abnormal High vs. Normal	Comparison	1,149		
			Background RH	346	0.79 (0.51,1.24)	0.308
			Low RH	207	1.59 (1.02,2.49)	0.042
			High RH	209	1.37 (0.86,2.18)	0.189
			Low plus High RH	416	1.48 (1.04,2.10)	0.030
16-4	RBC Count	Abnormal Low vs. Normal	Comparison	1,168		
			Background RH	350	1.14 (0.72,1.79)	0.575
			Low RH	210	0.70 (0.37,1.32)	0.266
			High RH	209	1.20 (0.63,2.30)	0.578
			Low plus High RH	419	0.91 (0.56,1.48)	0.715
		Abnormal High vs. Normal	Comparison	1,168		
			Background RH	350	1.06 (0.46,2.42)	0.895
			Low RH	210	0.84 (0.31,2.22)	0.719
			High RH	209	0.62 (0.21,1.81)	0.382
			Low plus High RH	419	0.72 (0.33,1.55)	0.402
16-6	WBC Count	Abnormal Low vs. Normal	Comparison	1,168		
			Background RH	350	0.89 (0.60,1.34)	0.578
			Low RH	210	0.70 (0.41,1.22)	0.210
			High RH	209	1.14 (0.67,1.94)	0.633
			Low plus High RH	419	0.90 (0.60,1.34)	0.590
		Abnormal High vs. Normal	Comparison	1,168		
			Background RH	350	1.34 (0.63,2.83)	0.443
			Low RH	210	0.36 (0.08,1.53)	0.165
			High RH	209	0.54 (0.16,1.83)	0.320
			Low plus High RH	419	0.44 (0.16,1.18)	0.102

Table G-23. *Summary of Adjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)*

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
16-8	Hemoglobin	Abnormal Low vs. Normal	Comparison	1,168		
			Background RH	350	1.01 (0.68,1.50)	0.964
			Low RH	210	0.81 (0.49,1.34)	0.406
			High RH	209	1.33 (0.82,2.16)	0.254
			Low plus High RH	419	1.04 (0.71,1.50)	0.856
		Abnormal High vs. Normal	Comparison	1,168		
			Background RH	350	0.86 (0.17,4.24)	0.854
			Low RH	210	0.53 (0.07,4.23)	0.552
			High RH	209	--	--
			Low plus High RH	419	--	--
16-10	Hematocrit	Abnormal Low vs. Normal	Comparison	1,168		
			Background RH	350	1.03 (0.59,1.78)	0.925
			Low RH	210	0.34 (0.12,0.97)	0.043
			High RH	209	1.37 (0.67,2.79)	0.382
			Low plus High RH	419	0.69 (0.36,1.32)	0.260
		Abnormal High vs. Normal	Comparison	1,168		
			Background RH	350	1.23 (0.31,4.87)	0.765
			Low RH	210	0.54 (0.07,4.28)	0.558
			High RH	209	0.71 (0.15,3.42)	0.668
			Low plus High RH	419	0.62 (0.16,2.43)	0.491
16-12	Platelet Count	Abnormal Low vs. Normal	Comparison	1,165		
			Background RH	349	1.18 (0.48,2.86)	0.719
			Low RH	210	0.73 (0.21,2.51)	0.616
			High RH	209	0.42 (0.09,1.89)	0.258
			Low plus High RH	419	0.55 (0.20,1.53)	0.254
		Abnormal High vs. Normal	Comparison	1,165		
			Background RH	349	0.83 (0.23,3.02)	0.777
			Low RH	210	--	--
			High RH	209	0.56 (0. 12,2.61)	0.463
			Low plus High RH	419	--	--

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
18-6	Diabetic Control (2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	Comparison	1,162		
			Background RH	349	0.38 (0.13,1.09)	0.071
			Low RH	206	1.74 (0.88,3.44)	0.110
			High RH	211	0.90 (0.38,2.12)	0.803
			Low plus High RH	417	1.24 (0.69,2.25)	0.469
		Diet and Exercise vs. Nondiabetic	Comparison	1,162		
			Background RH	349	0.88 (0.41,1.91)	0.746
			Low RH	206	0.97 (0.39,2.38)	0.944
			High RH	211	0.86 (0.32,2.31)	0.761
			Low plus High RH	417	0.91 (0.45,1.85)	0.796
		Oral Hypoglycemics vs. Nondiabetic	Comparison	1,162		
			Background RH	349	0.78 (0.46,1.31)	0.344
			Low RH	206	1.16 (0.69,1.95)	0.585
			High RH	211	1.19 (0.70,2.03)	0.517
			Low plus High RH	417	1.17 (0.79,1.75)	0.428
		Requiring Insulin vs. Nondiabetic	Comparison	1,162		
			Background RH	349	0.89 (0.37,2.12)	0.791
			Low RH	206	0.37 (0.09,1.61)	0.185
			High RH	211	2.66 (1.20,5.87)	0.016
			Low plus High RH	417	1.00 (0.42,2.39)	0.992
18-7	Diabetic Control (Pre-2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	Comparison	1,162		
			Background RH	349	0.69 (0.37,1.29)	0.241
			Low RH	206	1.06 (0.59,1.92)	0.838
			High RH	211	0.89 (0.47,1.69)	0.723
			Low plus High RH	417	0.97 (0.61,1.55)	0.905
		Diet and Exercise vs. Nondiabetic	Comparison	1,162		
			Background RH	349	0.98 (0.47,2.08)	0.966
			Low RH	206	0.93 (0.38,2.29)	0.876
			High RH	211	0.86 (0.32,2.32)	0.760
			Low plus High RH	417	0.89 (0.44,1.82)	0.754

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
	Diabetic Control (Pre-2002 AFHS Diabetes Definition) (continued)	Oral Hypoglycemics vs. Nondiabetic	Comparison	1,162		
			Background RH	349	0.79 (0.47,1.33)	0.378
			Low RH	206	1.10 (0.65,1.85)	0.728
			High RH	211	1.18 (0.69,2.02)	0.540
			Low plus High RH	417	1.14 (0.76,1.70)	0.522
		Requiring Insulin vs. Nondiabetic	Comparison	1,162		
			Background RH	349	0.90 (0.38,2.15)	0.813
			Low RH	206	0.35 (0.08,1.54)	0.165
			High RH	211	2.64 (1.19,5.83)	0.017
			Low plus High RH	417	0.98 (0.41,2.33)	0.959
18-13	TSH	Abnormal Low vs. Normal	Comparison	1,089		
			Background RH	327	--	--
			Low RH	201	--	--
			High RH	203	0.84 (0.09,7.63)	0.873
			Low plus High RH	404	--	--
		Abnormal High vs. Normal	Comparison	1,089		
			Background RH	327	1.71 (0.82,3.57)	0.152
			Low RH	201	1.20 (0.45,3.24)	0.714
			High RH	203	1.41 (0.50,3.95)	0.511
			Low plus High RH	404	1.30 (0.60,2.82)	0.500
18-23	Fasting Insulin	Abnormal Low vs. Normal	Comparison	1,162		
			Background RH	349	0.81 (0.53,1.22)	0.309
			Low RH	206	0.85 (0.47,1.55)	0.598
			High RH	211	0.54 (0.25,1.14)	0.105
			Low plus High RH	417	0.67 (0.41,1.11)	0.123
		Abnormal High vs. Normal	Comparison	1,162		
			Background RH	349	1.32 (0.74,2.35)	0.341
			Low RH	206	1.26 (0.69,2.29)	0.449
			High RH	211	1.64 (0.95,2.82)	0.076
			Low plus High RH	417	1.44 (0.92,2.24)	0.107

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
18-25	2-hour Postprandial Insulin (Nondiabetics Only)	Abnormal Low vs. Normal	Comparison	931		
			Background RH	305	1.45 (0.83,2.54)	0.187
			Low RH	158	0.79 (0.30,2.09)	0.631
			High RH	159	1.30 (0.55,3.07)	0.547
			Low plus High RH	317	1.01 (0.51,2.01)	0.970
		Abnormal High vs. Normal	Comparison	931		
			Background RH	305	0.98 (0.73,1.31)	0.884
			Low RH	158	0.82 (0.56,1.19)	0.299
			High RH	159	0.87 (0.59,1.29)	0.494
			Low plus High RH	317	0.85 (0.63,1.13)	0.254
20-13	Loss of Vital Capacity	Mild vs. None	Comparison	1,156		
			Background RH	347	0.53 (0.27,1.07)	0.075
			Low RH	206	0.95 (0.53,1.71)	0.870
			High RH	211	0.68 (0.35,1.32)	0.251
			Low plus High RH	417	0.80 (0.50,1.29)	0.362
		Moderate or Severe vs. None	Comparison	1,156		
			Background RH	347	1.15 (0.45,2.96)	0.766
			Low RH	206	1.06 (0.40,2.82)	0.904
			High RH	211	0.40 (0.09,1.79)	0.231
			Low plus High RH	417	0.65 (0.25,1.67)	0.369
20-14	Obstructive Abnormality	Mild vs. None	Comparison	1,155		
			Background RH	347	1.00 (0.76,1.31)	0.993
			Low RH	206	1.21 (0.86,1.69)	0.282
			High RH	211	0.89 (0.62,1.28)	0.525
			Low plus High RH	417	1.03 (0.79,1.35)	0.810
		Moderate vs. None	Comparison	1,155		
			Background RH	347	0.85 (0.51,1.43)	0.541
			Low RH	206	1.12 (0.64,1.96)	0.691
			High RH	211	0.57 (0.29,1.12)	0.102
			Low plus High RH	417	0.80 (0.50,1.27)	0.339

Table G-23. Summary of Adjusted Results for Polytomous Variables – Model 3 (Ranch Hands and Comparisons by Dioxin Category) (Continued)

Table Ref.	Clinical Parameter	Contrast	Dioxin Category	n	Adjusted Relative Risk (95% C.I.)[a]	p-Value
	Obstructive Abnormality (continued)	Severe vs. None	Comparison	1,155		
			Background RH	347	1.16 (0.55,2.47)	0.692
			Low RH	206	1.71 (0.77,3.77)	0.184
			High RH	211	0.27 (0.06,1.18)	0.082
			Low plus High RH	417	0.67 (0.27,1.62)	0.372

[a]Relative risk and confidence interval relative to Comparisons.

--: Relative risk, confidence interval, and p-value were not presented because of the sparse number of participants with abnormalities.

Note: RH = Ranch Hand.
Background: (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Table G-24. Summary of Adjusted Results for Polytomous Variables – Model 4 (Ranch Hands: Log$_2$ (1987 Dioxin))

Table Ref.	Clinical Parameter	Contrast	Adjusted Relative Risk (95% C.I.)[a]	p-Value
11-24	Patellar Reflex	Active or Very Active vs. Sluggish or Absent	1.04 (0.92,1.19)	0.526
		Sluggish, Active, or Very Active vs. Absent	1.44 (1.07,1.95)	0.013
11-25	Achilles Reflex	Active or Very Active vs. Sluggish or Absent	0.98 (0.87,1.10)	0.738
		Sluggish, Active, or Very Active vs. Absent	1.03 (0.90,1.18)	0.671
11-26	Biceps Reflex	Active or Very Active vs. Sluggish or Absent	1.06 (0.94,1.20)	0.332
		Sluggish, Active, or Very Active vs. Absent	1.19 (0.85,1.68)	0.302
13-47	α-1-Antitrypsin	Abnormal Low vs. Normal	0.73 (0.46,1.19)	0.207
		Abnormal High vs. Normal	1.11 (0.96,1.29)	0.149
16-4	RBC Count	Abnormal Low vs. Normal	0.98 (0.78,1.24)	0.882
		Abnormal High vs. Normal	1.04 (0.73,1.48)	0.824
16-6	WBC Count	Abnormal Low vs. Normal	1.05 (0.86,1.27)	0.655
		Abnormal High vs. Normal	0.61 (0.43,0.86)	0.005
16-8	Hemoglobin	Abnormal Low vs. Normal	1.03 (0.88,1.21)	0.687
		Abnormal High vs. Normal	0.64 (0.25,1.67)	0.365
16-10	Hematocrit	Abnormal Low vs. Normal	1.02 (0.77,1.37)	0.867
		Abnormal High vs. Normal	1.12 (0.61,2.07)	0.705
16-12	Platelet Count	Abnormal Low vs. Normal	0.91 (0.55,1.51)	0.722
		Abnormal High vs. Normal	0.67 (0.37,1.22)	0.191
18-6	Diabetic Control (2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	1.17 (0.83,1.64)	0.365
		Diet and Exercise vs. Nondiabetic	1.00 (0.71,1.42)	0.987
		Oral Hypoglycemics vs. Nondiabetic	1.32 (1.08,1.60)	0.006
		Requiring Insulin vs. Nondiabetic	1.53 (1.07,2.19)	0.021
18-7	Diabetic Control (Pre-2002 AFHS Diabetes Definition)	No Treatment vs. Nondiabetic	1.17 (0.90,1.52)	0.238
		Diet and Exercise vs. Nondiabetic	0.97 (0.69,1.37)	0.867
		Oral Hypoglycemics vs. Nondiabetic	1.32 (1.09,1.61)	0.005
		Requiring Insulin vs. Nondiabetic	1.54 (1.07,2.21)	0.019
18-13	TSH	Abnormal Low vs. Normal	2.13 (0.72,6.30)	0.171
		Abnormal High vs. Normal	0.93 (0.70,1.24)	0.633
18-23	Fasting Insulin	Abnormal Low vs. Normal	1.01 (0.82,1.25)	0.909
		Abnormal High vs. Normal	1.21 (0.97,1.51)	0.091
18-25	2-hour Postprandial Insulin (Nondiabetics Only)	Abnormal Low vs. Normal	0.94 (0.72,1.23)	0.668
		Abnormal High vs. Normal	1.02 (0.89,1.17)	0.777
20-13	Loss of Vital Capacity	Mild vs. None	1.05 (0.82,1.35)	0.683
		Moderate or Severe vs. None	0.85 (0.57,1.28)	0.447
20-14	Obstructive Abnormality	Mild vs. None	0.99 (0.88,1.12)	0.901
		Moderate vs. None	0.99 (0.80,1.24)	0.960
		Severe vs. None	0.79 (0.57,1.11)	0.177

[a]Relative risk for a twofold increase in 1987 dioxin.

APPENDIX H

APPENDIX H. SIGNIFICANT ADJUSTED GROUP AND DIOXIN ANALYSES

This appendix contains a summary of significant results ($p \leq 0.05$) for the adjusted analyses that were performed for the group and dioxin analyses (Models 1-4) in Chapters 9 through 20. The dependent variable and its table reference are listed along with the model and the contrast or description of the model. The p-value is provided along with analysis statistics that correspond to the type of analysis that was performed (either continuous or discrete). A description of the analysis and the statistics that are presented is referenced under the "Note" column and is explained in footnotes.

List of Tables

Table H-1. Summary of Results from Significant Adjusted Analyses in the General Health Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Body Mass Index (9-6)	3	Background RH vs. C	<0.001	-1.04	RH: 27.81 kg/m^2 C: 28.85 kg/m^2	(a)
	3	Low RH vs. C	0.006	0.87	RH: 29.72 kg/m^2 C: 28.85 kg/m^2	(a)
	3	High RH vs. C	<0.001	1.15	RH: 30.00 kg/m^2 C: 28.85 kg/m^2	(a)
	3	Low plus High RH vs. C	<0.001	1.01	RH: 29.86 kg/m^2 C: 28.85 kg/m^2	(a)
	4	All RH: 1987 Dioxin	<0.001	0.026 (0.004)	Low: 26.93 kg/m^2 Medium: 28.88 kg/m^2 High: 29.65 kg/m^2	(b)
Body Mass Index (9-7)	3	Background RH vs. C	<0.001	0.59 (0.45,0.79)	RH: 23.1% C: 35.3%	(c)
	3	Low RH vs. C	0.011	1.48 (1.09,2.01)	RH: 44.1% C: 35.3%	(c)
	3	High RH vs. C	0.009	1.52 (1.11,2.07)	RH: 46.9% C: 35.3%	(c)
	3	Low plus High RH vs. C	0.001	1.50 (1.19,1.89)	RH: 45.5% C: 35.3%	(c)
	4	All RH: 1987 Dioxin	<0.001	1.31 (1.17,1.47)	Low: 21.6% Medium: 38.0% High: 46.5%	(d)

(a): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was performed on natural logarithm scale; adjusted means were transformed to original scale and were presented for each dioxin category in contrast.

(b): Continuous variable: slope and standard error were presented and were based on natural logarithm of dependent variable versus $\log_2$ (1987 dioxin); adjusted means were transformed to original scale and were presented for each of three 1987 dioxin categories.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

Note: RH = Ranch Hand.
C = Comparison.

Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Model 4:   Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

Table H-2. Summary of Results from Significant Adjusted Analyses in the Neoplasia Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Percent Abnormal	Note
All Skin Neoplasms (10-3)	1	RH vs. C, All	0.012	1.28 (1.06,1.56)	RH: 54.2% C: 47.8%	(a)
	3	Low RH vs. C	0.007	1.56 (1.13,2.17)	RH: 61.0% C: 47.8%	(b)
	3	Low plus High RH vs. C	0.026	1.32 (1.03,1.68)	RH: 54.2% C: 47.8%	(b)
Malignant Skin Neoplasms (10-4)	3	Low RH vs. C	0.024	1.52 (1.06,2.19)	RH: 31.6% C: 21.5%	(b)
Skin Neoplasms of Uncertain Behavior or Unspecified Nature (10-6)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.033	0.23 (0.04,1.38)	Low: 2.4% Medium: 0.8% High: 0.0%	(c)
	3	Low RH vs. C	0.041	4.14 (1.06,16.16)	RH: 2.1% C: 0.5%	(b)
Basal Cell Carcinoma (All Sites Combined) (10-7)	1	RH vs. C, All	0.027	1.33 (1.03,1.71)	RH: 21.4% C: 16.9%	(a)
	1	RH vs. C, Officer	0.013	1.58 (1.10,2.27)	RH: 28.0% C: 19.4%	(a)
	3	Low RH vs. C	0.010	1.66 (1.13,2.43)	RH: 26.7% C: 16.9%	(b)
Nonmelanoma (10-9)	1	RH vs. C, All	0.027	1.31 (1.03,1.67)	RH: 24.3% C: 19.6%	(a)
	1	RH vs. C, Officer	0.032	1.46 (1.03,2.07)	RH: 30.7% C: 23.0%	(a)
	3	Low RH vs. C	0.013	1.60 (1.10,2.31)	RH: 29.9% C: 19.6%	(b)
Malignant Systemic Neoplasms (10-12)	1	RH vs. C, Officer	0.014	1.81 (1.13,2.91)	RH: 16.6% C: 10.8%	(a)
	3	Low RH vs. C	0.003	2.05 (1.28,3.26)	RH: 19.4% C: 10.1%	(b)
Malignant Systemic Neoplasms (Oral Cavity, Pharynx, and Larynx) (10-17)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.010	0.12 (0.01,1.09)	Low: 2.9% Medium: 0.0% High: 0.0%	(c)
Malignant Systemic Neoplasms (Thymus, Heart, and Mediastinum) (10-18)	4	All RH: 1987 Dioxin	0.009	0.04 (0.00,7.74)	Low: 0.8% Medium: 0.0% High: 0.0%	(d)
Malignant Systemic Neoplasms (Bronchus and Lung) (10-20)	3	Low RH vs. C	0.024	3.91 (1.20,12.74)	RH: 3.9% C: 0.6%	(b)
Malignant Systemic Neoplasms (Colon and Rectum) (10-22)	1	RH vs. C, Officer	0.044	4.66 (1.04,20.80)	RH: 2.6% C: 0.7%	(a)
	3	Low RH vs. C	0.035	3.74 (1.10,12.73)	RH: 3.4% C: 0.9%	(b)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Percent Abnormal	Note
Malignant Systemic Neoplasms (Urinary System) (10-23)	1	RH vs. C, All	0.018	3.02 (1.16,7.89)	RH: 2.3% C: 1.0%	(a)
	1	RH vs. C, Officer	0.049	3.59 (1.01,12.81)	RH: 2.6% C: 1.1%	(a)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.049	2.08 (0.99,4.37)	Low: 1.5% Medium: 2.8% High: 2.1%	(c)
	3	Background RH vs. C	0.018	3.62 (1.24,10.51)	RH: 2.6% C: 1.0%	(b)
Malignant Systemic Neoplasms (Kidney and Ureter (10-24)	4	All RH: 1987 Dioxin	0.048	0.55 (0.31,0.98)	Low: 1.2% Medium: 0.4% High: 1.2%	(d)
Malignant Systemic Neoplasms (Prostate) (10-25)	3	Low RH vs. C	0.048	1.85 (1.00,3.39)	RH: 10.7% C: 5.7%	(b)
Malignant Systemic Neoplasms (Penis and Other Male Genital) (10-26)	4	All RH: 1987 Dioxin	0.017	3.52 (1.04,11.91)	Low: 0.0% Medium: 0.0% High: 0.8%	(d)
Carcinoma in Situ (10-30)	3	Low RH vs. C	0.027	20.75 (1.40,307.55)	RH: 1.5% C: 0.5%	(b)
Leukemia (10-32)	4	All RH: 1987 Dioxin	0.004	0.40 (0.21,0.74)	Low: 1.2% Medium: 0.4% High: 0.0%	(d)
Skin and Systemic Neoplasms (10-35)	3	Low RH vs. C	0.048	1.46 (1.00,2.12)	RH: 73.8% C: 61.7%	(b)
Malignant Skin and Systemic Neoplasms (10-36)	3	Low RH vs. C	0.008	1.64 (1.14,2.37)	RH: 41.4% C: 27.4%	(b)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal is presented for each exposure group in contrast.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal is presented for each dioxin category in contrast.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal is presented for each of three initial dioxin categories.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal is presented for each of three 1987 dioxin categories.

Note: RH = Ranch Hand.
C = Comparison.

Model 2: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt).

Model 3: Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Model 4: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

Table H-3. Summary of Results from Significant Adjusted Analyses in the Neurology Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Percent Abnormal	Note
Hereditary and Degenerative Diseases (11-4)	1	RH vs. C, Officer	0.030	1.57 (1.04,2.36)	RH: 18.6% C: 12.4%	(a)
Smell (11-7)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.007	0.30 (0.10,0.89)	Low: 3.6% Medium: 2.1% High: 0.0%	(b)
	4	All RH: 1987 Dioxin	0.010	0.64 (0.45,0.90)	Low: 4.6% Medium: 2.7% High: 0.8%	(c)
Visual Fields (11-8)	1	RH vs. C, All	0.022	3.08 (1.13,8.41)	RH: 1.6% C: 0.6%	(a)
	3	Background RH vs. C	0.004	5.25 (1.71,16.13)	RH: 2.3% C: 0.6%	(d)
Facial Sensation (11-11)	3	Low RH vs. C	0.033	7.94 (1.19,53.10)	RH: 1.4% C: 0.3%	(d)
Balance (11-15)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.033	2.11 (1.03,4.34)	Low: 2.9% Medium: 2.1% High: 2.9%	(b)
Cranial Nerve Index (11-20)	1	RH vs. C, All	0.020	1.47 (1.06,2.04)	RH: 10.7% C: 7.7%	(a)
	3	Background RH vs. C	0.018	1.65 (1.09,2.50)	RH: 11.5% C: 7.7%	(d)
	3	Low RH vs. C	0.049	1.62 (1.00,2.61)	RH: 12.4% C: 7.7%	(d)
Pinprick (11-21)	3	High RH vs. C	0.050	1.71 (1.00,2.93)	RH: 15.3% C: 8.9%	(d)
Patellar Reflex (11-24)	3	High RH vs. C – Absent vs. Very Active, Active, or Sluggish	0.048	2.11 (1.01,4.43)	RH: 5.7% C: 3.0%	(d)
	3	Low and High RH vs. C – Absent vs. Very Active, Active, or Sluggish	0.027	1.89 (1.07,3.33)	RH: 5.7% C: 3.0%	(d)
	4	All RH: 1987 Dioxin – Absent vs. Very Active, Active, or Sluggish	0.013	1.44 (1.07,1.95)	Low: 2.3% Medium: 5.5% High: 5.1%	(c)
Achilles Reflex (11-25)	1	RH vs. C, Officer – Sluggish or Absent vs. Very Active or Active	0.031	1.42 (1.03,1.95)	RH: 66.0% C: 57.1%	(a)
Coordination (11-32)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.002	2.25 (1.30,3.90)	Low: 2.9% Medium: 2.1% High: 5.8%	(b)
Romberg Sign (11-33)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.033	2.11 (1.03,4.34)	Low: 2.9% Medium: 2.1% High: 2.9%	(b)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal was presented for each of three initial dioxin categories.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

Note: RH = Ranch Hand.
           C = Comparison.

        Model 2:   Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt).

        Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
                       Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
                       High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

        Model 4:   Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

Table H-4. Summary of Results from Significant Adjusted Analyses in the Psychology Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Other Neuroses (12-7)	1	RH vs. C, Officer	0.043	0.73 (0.54,0.99)	RH: 43.5% C: 51.5%	(a)
SCL-90-R Interpersonal Sensitivity (12-11)	1	RH vs. C, All	0.013	0.65 (0.46,0.92)	RH: 7.4% C: 10.7%	(a)
	1	RH vs. C, Officer	0.045	0.47 (0.23,0.98)	RH: 3.3% C: 6.7%	(a)
	3	Low RH vs. C	0.011	0.40 (0.20,0.81)	RH: 4.8% C: 10.7%	(b)
	3	Low plus High RH vs. C	0.013	0.56 (0.36,0.88)	RH: 7.9% C: 10.7%	(b)
SCL-90-R Paranoid Ideation (12-13)	1	RH vs. C, All	0.011	0.53 (0.32,0.88)	RH: 3.1% C: 5.6%	(a)
	1	RH vs. C, Enlisted Groundcrew	0.033	0.51 (0.27,0.95)	RH: 4.8% C: 8.8%	(a)
	3	Low plus High RH vs. C	0.019	0.45 (0.23,0.88)	RH: 3.3% C: 5.6%	(b)
SCL-90-R Phobic Anxiety (12-14)	4	All RH: 1987 Dioxin	0.014	0.80 (0.66,0.96)	Low: 6.9% Medium: 5.4% High: 9.1%	(c)
SCL-90-R Positive Symptom Total (PST) (12-18)	1	RH vs. C, All	0.033	0.72 (0.53,0.98)	RH: 9.6% C: 12.6%	(a)
	3	Low RH vs. C	0.019	0.49 (0.27,0.89)	RH: 6.7% C: 12.6%	(b)
	3	Low plus High RH vs. C	0.025	0.64 (0.43,0.94)	RH: 10.5% C: 12.6%	(b)

Table H-4. Summary of Results from Significant Adjusted Analyses in the Psychology Assessment (Continued)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
SCL-90-R Positive Symptom Distress Index (PSDI) (12-19)	1	RH vs. C, Enlisted Flyer	0.036	0.43 (0.20,0.95)	RH: 7.5% C: 15.1%	(a)
WMS-R Logical Memory, Delayed Recall (12-22)[a]	1	RH vs. C, Enlisted Groundcrew	0.039	0.50 (0.02,0.97)	RH: 8.46 C: 7.97	(d)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

(d): Continuous variable: difference of adjusted means and 95% confidence interval was presented; adjusted means were presented for each exposure group in contrast.

[a]A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: RH = Ranch Hand.
C = Comparison.

Model 3:   Background (Ranch Hand): 1987 dioxin $\leq$ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin $\leq$ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Model 4:   Low = $\leq$7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

Table H-5. Summary of Results from Significant Adjusted Analyses in the Gastrointestinal Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Unspecified Jaundice (13-4)	3	Low plus High RH vs. C	0.027	0.24 (0.07,0.85)	RH: 0.7% C: 2.9%	(a)
	4	All RH: 1987 Dioxin	0.014	0.59 (0.39,0.90)	Low: 3.2% Medium: 2.0% High: 0.4%	(b)
Alkaline Phosphatase (13-18)	1	RH vs. C, Enlisted Groundcrew	0.039	1.70 (1.03,2.80)	RH: 10.6% C: 6.4%	(c)
Direct Bilirubin (13-21)	1	RH vs. C, All	0.041	0.24 (0.05,1.14)	RH: 0.3% C: 1.0%	(c)
Cholesterol (13-25)	3	Low plus High RH vs. C	0.039	0.68 (0.47,0.98)	RH: 10.3% C: 13.3%	(a)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Triglycerides (13-31)	1	RH vs. C, All	0.023	1.40 (1.05,1.88)	RH: 13.4% C: 9.8%	(c)
	1	RH vs. C, Enlisted Groundcrew	0.034	1.54 (1.03,2.29)	RH: 17.9% C: 11.9%	(c)
	3	Low RH vs. C	0.015	1.72 (1.11,2.66)	RH: 15.4% C: 9.8%	(a)
	3	High RH vs. C	0.012	1.70 (1.12,2.57)	RH: 20.4% C: 9.8%	(a)
	3	Low plus High RH vs. C	0.001	1.71 (1.23,2.38)	RH: 17.9% C: 9.8%	(a)
	4	All RH: 1987 Dioxin	0.020	1.20 (1.03,1.40)	Low: 6.3% Medium: 12.9% High: 21.2%	(b)
Serum Amylase (13-34)	1	RH vs. C, Officer	0.049	-3.25	RH: 57.85 U/L C: 61.10 U/L	(d)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.031	-0.036 (0.017)	Low: 63.07 U/L Medium: 57.35 U/L High: 57.06 U/L	(e)
	4	All RH: 1987 Dioxin	0.048	-0.020 (0.010)	Low: 63.87 U/L Medium: 62.03 U/L High: 58.26 U/L	(f)
Serum Amylase (13-35)	1	RH vs. C, Officer	0.038	0.27 (0.08,0.93)	RH: 1.0% C: 3.5%	(c)
Prior Hepatitis B Infection (13-37)	1	RH vs. C, All	<0.001	0.53 (0.38,0.76)	RH: 6.4% C: 11.0%	(c)
	1	RH vs. C, Officer	0.034	0.40 (0.17,0.93)	RH: 2.3% C: 5.4%	(c)
	1	RH vs. C, Enlisted Groundcrew	0.016	0.56 (0.35,0.90)	RH: 8.3% C: 13.7%	(c)
	3	Background RH vs. C	0.004	0.44 (0.25,0.77)	RH: 4.3% C: 11.0%	(a)
	3	Low RH vs. C	0.045	0.56 (0.31,0.99)	RH: 7.1% C: 11.0%	(a)
	3	Low plus High RH vs. C	0.012	0.59 (0.40,0.89)	RH: 8.3% C: 11.0%	(a)
Antibodies for Hepatitis C (13-38)	1	RH vs. C, All	0.037	0.37 (0.13,1.02)	RH: 0.6% C: 1.6%	(c)
Stool Hemoccult (13-39)	1	RH vs. C, Officer	0.043	8.99 (1.07,75.33)	RH: 2.1% C: 0.2%	(c)
Albumin (13-43)	4	All RH: 1987 Dioxin	0.030	0.37 (0.15,0.94)	Low: 1.6% Medium: 0.4% High: 0.0%	(b)
α-1-Acid Glycoprotein (13-44)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	<0.001	-0.038 (0.010)	Low: 76.97 mg/dL Medium: 76.46 mg/dL High: 71.12 mg/dL	(e)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
α-1-Antitrypsin (13-47)	3	Low RH vs. C – Abnormal High vs. Normal	0.042	1.59 (1.02,2.49)	RH: 14.4% C: 9.9%	(a)
	3	Low plus High RH vs. C – Abnormal High vs. Normal	0.030	1.48 (1.04,2.10)	RH: 14.1% C: 9.9%	(a)
C3 Complement[a] (13-52)	3	Low RH vs. C	0.011	3.8	RH: 124.2 mg/dL C: 120.4 mg/dL	(g)
C4 Complement[a] (13-54)	1	RH vs. C, Officer	0.032	-0.91	RH: 23.56 mg/dL C: 24.46 mg/dL	(d)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.041	-0.053 (0.026)	Low: 23.52 mg/dL Medium: 24.47 mg/dL High: 22.90 mg/dL	(h)
C4 Complement (13-55)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	<0.001	1.80 (1.26,2.57)	Low: 5.8% Medium: 3.5% High: 11.4%	(i)
Haptoglobin (13-56)	1	RH vs. C, All	0.026	6.0	RH: 123.3 mg/dL C: 117.3 mg/dL	(d)
	1	RH vs. C, Enlisted Groundcrew	0.031	9.1	RH: 132.6 mg/dL C: 123.4 mg/dL	(d)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.043	-0.227 (0.112)	Low: 114.7 mg/dL Medium: 120.4 mg/dL High: 107.7 mg/dL	(h)
	3	Low plus High RH vs. C	0.040	6.9	RH: 124.2 mg/dL C: 117.3 mg/dL	(g)
Haptoglobin (13-57)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.026	0.75 (0.58,0.97)	Low: 13.0% Medium: 19.9% High: 10.7%	(i)
Transferrin[a] (13-58)	3	Low RH vs. C	0.027	6.7	RH: 254.3 mg/dL C: 247.6 mg/dL	(g)
Transferrin (13-59)	3	Low RH vs. C	0.041	0.41 (0.18,0.97)	RH: 2.9% C: 6.2%	(a)
	3	Low plus High RH vs. C	0.029	0.50 (0.27,0.93)	RH: 3.1% C: 6.2%	(a)
Prothrombin Time (13-60)	3	Background RH vs. C	0.042	0.07	RH: 10.79 seconds C: 10.72 seconds	(g)
	4	All RH: 1987 Dioxin	0.050	-0.003 (0.001)	Low: 10.79 seconds Medium: 10.73 seconds High: 10.66 seconds	(f)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

Table H-5. Summary of Results from Significant Adjusted Analyses in the Gastrointestinal Assessment (Continued)

(d): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each exposure group in contrast.

(e): Continuous variable: slope and standard error were presented and were based on the natural logarithm of the dependent variable versus $\log_2$ (initial dioxin); adjusted means were presented for each of three initial dioxin categories.

(f): Continuous variable: slope and standard error were presented and were based on the natural logarithm of the dependent variable versus $\log_2$ (1987 dioxin); adjusted means were presented for each of three 1987 dioxin categories.

(g): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each dioxin category in contrast.

(h): Continuous variable: slope and standard error were presented and were based on the square root of the dependent variable versus $\log_2$ (initial dioxin); adjusted means were presented for each of three initial dioxin categories.

(i): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal was presented for each of three initial dioxin categories.

[a]A negative difference in means (Ranch Hand mean less than Comparison mean) was considered adverse to Ranch Hands for this variable. A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: RH = Ranch Hand.
        C = Comparison.

Model 2:   Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt).

Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
            Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
            High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Model 4:   Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

Table H-6. Summary of Results from Significant Adjusted Analyses in the Dermatology Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Occurrence of Acne (Lifetime) (14-3)	1	RH vs. C, All	0.002	1.34 (1.11,1.61)	RH: 47.5% C: 40.6%	(a)
	1	RH vs. C, Enlisted Groundcrew	<0.001	1.61 (1.22,2.14)	RH: 52.8% C: 40.6%	(a)
	3	Low RH vs. C	0.002	1.63 (1.20,2.20)	RH: 50.2% C: 40.6%	(b)
	3	Low plus High RH vs. C	0.002	1.45 (1.15,1.83)	RH: 49.8% C: 40.6%	(b)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Post-SEA Acne (14-4)	1	RH vs. C, All	0.001	1.43 (1.15,1.78)	RH: 26.4% C: 20.4%	(a)
	1	RH vs. C, Enlisted Groundcrew	0.003	1.60 (1.18,2.16)	RH: 35.0% C: 24.9%	(a)
	3	Background RH vs. C	0.009	1.49 (1.10,2.01)	RH: 23.9% C: 20.4%	(b)
	3	Low RH vs. C	0.003	1.68 (1.19,2.37)	RH: 27.5% C: 20.4%	(b)
	3	Low plus High RH vs. C	0.011	1.41 (1.08,1.83)	RH: 28.3% C: 20.4%	(b)
Post-SEA Acne (no pre-SEA acne) (14-5)	1	RH vs. C, All	<0.001	1.78 (1.29,2.46)	RH: 18.0% C: 11.4%	(a)
	1	RH vs. C, Enlisted Groundcrew	<0.001	2.15 (1.40,3.29)	RH: 26.3% C: 14.2%	(a)
	3	Background RH vs. C	0.046	1.60 (1.01,2.53)	RH: 14.1% C: 11.4%	(b)
	3	Low RH vs. C	0.002	2.19 (1.34,3.58)	RH: 20.5% C: 11.4%	(b)
	3	High RH vs. C	0.026	1.72 (1.07,2.78)	RH: 22.1% C: 11.4%	(b)
	3	Low plus High RH vs. C	<0.001	1.93 (1.33,2.82)	RH: 21.3% C: 11.4%	(b)
Duration of Post-SEA Acne (no pre-SEA acne) (14-11)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	<0.001	1.808 (0.455)	Low: 17.75 months Medium: 33.79 months High: 102.59 months	(c)
	3	High RH vs. C	0.002	54.28	RH: 104.25 months C: 49.97 months	(d)
	4	All RH: 1987 Dioxin	0.002	0.964 (0.294)	Low: 29.90 months Medium: 27.36 months High: 65.97 months	(e)
Acneiform Lesions (14-13)	3	Background RH vs. C	0.042	1.72 (1.02,2.90)	RH: 6.5% C: 4.9%	(b)
Comedones (14-15)	1	RH vs. C, Officer	0.049	0.46 (0.21,1.00)	RH: 2.9% C: 6.1%	(a)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(c): Continuous variable: slope and standard error were presented and were based on square root of dependent variable versus $\log_2$ (initial dioxin); adjusted means were transformed to original scale and were presented for each of three initial dioxin categories.

(d): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were transformed to original scale and were presented for each dioxin category in contrast.

(e): Continuous variable: slope and standard error were presented and were based on square root of dependent variable versus $\log_2$ (1987 dioxin); adjusted means were transformed to original scale and were presented for each of three 1987 dioxin categories.

Table H-6. Summary of Results from Significant Adjusted Analyses in the Dermatology Assessment (Continued)

Note: RH = Ranch Hand.
C = Comparison.

Model 2:   Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt).

Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Model 4:   Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

Table H-7. Summary of Results from Significant Adjusted Analyses in the Cardiovascular Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Heart Disease (Excluding Essential Hypertension) (15-4)	1	RH vs. C, Enlisted Flyer	0.015	2.46 (1.19,5.11)	RH: 91.6% C: 81.0%	(a)
Systolic Blood Pressure (Continuous) (15-7)	3	Low RH vs. C	0.025	-2.9	RH: 127.6 mm Hg C: 130.5 mm Hg	(b)
	3	Low plus High RH vs. C	0.022	-2.3	RH: 128.2 mm Hg C: 130.5 mm Hg	(b)
Systolic Blood Pressure (Discrete) (15-8)	3	Low RH vs. C	0.018	0.63 (0.43,0.92)	RH: 19.4% C: 26.0%	(c)
	3	Low plus High RH vs. C	0.023	0.72 (0.54,0.96)	RH: 20.3% C: 26.0%	(c)
	4	All RH: 1987 Dioxin	0.023	0.86 (0.75,0.98)	Low: 26.2% Medium: 21.7% High: 20.7%	(d)
Diastolic Blood Pressure (Discrete) (15-10)	3	High RH vs. C	0.036	1.88 (1.04,3.39)	RH: 9.0% C: 4.8%	(c)
Posterior Tibial Pulses (15-26)	1	RH vs. C, All	0.027	0.59 (0.36,0.95)	RH: 4.3% C: 5.9%	(a)
	1	RH vs. C, Officer	0.047	0.46 (0.22,0.99)	RH: 3.6% C: 6.9%	(a)
	3	Background RH vs. C	0.039	0.48 (0.24,0.96)	RH: 4.0% C: 5.9%	(c)
	3	Low RH vs. C	0.048	0.40 (0.16,0.99)	RH: 3.4% C: 5.9%	(c)
Peripheral Pulses (15-28)	3	Low RH vs. C	0.046	0.61 (0.37,0.99)	RH: 10.8% C: 15.9%	(c)

Table H-7. Summary of Results from Significant Adjusted Analyses in the Cardiovascular Assessment (Continued)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(b): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each dioxin category in contrast.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

Note: RH = Ranch Hand.
C = Comparison.

Model 3: Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Model 4: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

Table H-8. Summary of Results from Significant Adjusted Analyses in the Hematology Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
WBC Count (16-5)	4	All RH: 1987 Dioxin	0.047	-0.014 (0.007)	Low: 5.98 thousand/mm^3 Medium: 5.81 thousand/mm^3 High: 5.83 thousand/mm^3	(a)
WBC Count (16-6)	4	All RH: 1987 Dioxin – Abnormal High vs. Normal	0.005	0.61 (0.43,0.86)	Low: 2.7% Medium: 1.9% High: 1.6%	(b)
Hematocrit (16-10)	3	Low RH vs. C: Abnormal Low vs. Normal	0.043	0.34 (0.12,0.97)	RH: 1.9% C: 5.1%	(c)
Platelet Count (16-11)	1	RH vs. C, Enlisted Flyer	0.005	18.4	RH: 249.5 thousand/mm^3 C: 231.1 thousand/mm^3	(d)
RBC Morphology (16-13)	1	RH vs. C, Enlisted Groundcrew	0.022	2.10 (1.12,3.97)	RH: 6.9% C: 3.8%	(e)
	3	High RH vs. C	0.047	1.93 (1.01,3.70)	RH: 6.7% C: 5.2%	(c)
	3	Low plus High RH vs. C	0.021	1.74 (1.09,2.78)	RH: 7.6% C: 5.2%	(c)
ESR (16-25)	3	Low plus High RH vs. C	0.027	0.99	RH: 8.80 mm/hour C: 7.81 mm/hour	(f)

Table H-8. Summary of Results from Significant Adjusted Analyses in the Hematology Assessment (Continued)

(a): Continuous variable: slope and standard error were presented and were based on natural logarithm of dependent variable versus $\log_2$ (initial dioxin); adjusted means were presented for each of three 1987 dioxin categories.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(d): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each exposure group in contrast.

(e): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(f): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each dioxin category in contrast.

Note: RH = Ranch Hand.
C = Comparison.

Model 3: Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Model 4: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

Table H-9. Summary of Results from Significant Adjusted Analyses in the Renal Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Serum Creatinine (17-6)	1	RH vs. C, All	0.031	-0.02	RH: 1.17 mg/dL C: 1.19 mg/dL	(a)
	1	RH vs. C, Officer	0.010	-0.04	RH: 1.16 mg/dL C: 1.20 mg/dL	(a)
Creatinine Clearance (17-7)	3	Low RH vs. C	0.015	2.92	RH: 85.27 C: 82.35	(b)
	3	Low plus High RH vs. C	0.014	2.26	RH: 84.61 C: 82.35	(b)
	4	All RH: 1987 Dioxin	<0.001	0.118 (0.025)	Low: 79.36 Medium: 85.48 High: 86.92	(c)
Urinary Microalbumin to Urinary Creatinine Ratio (17-8)	1	RH vs. C, All	0.037	-12.69	RH: 27.44 µg/mg C: 40.13 µg/mg	(a)
	1	RH vs. C, Enlisted Groundcrew	0.024	-19.06	RH: 23.85 µg/mg C: 42.91 µg/mg	(a)
	3	Low RH vs. C	0.033	-16.47	RH: 22.00 µg/mg C: 38.47 µg/mg	(b)

(a): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were transformed to original scale and were presented for each exposure group in contrast.

(b): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were transformed to original scale and were presented for each dioxin category in contrast.

(c): Continuous variable: slope and standard error were presented and were based on square root of dependent variable versus $\log_2$ (1987 dioxin); adjusted means were transformed to original scale and were presented for each of three 1987 dioxin categories.

Note: RH = Ranch Hand.
C = Comparison.

Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Model 4:   Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

Table H-10. Summary of Results from Significant Adjusted Analyses in the Endocrinology Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p–Value	Analysis Statistics	Adjusted Mean or Percent Abnormal		Note
Composite Diabetes Indicator (2002 AFHS diabetes definition) (18-4)	4	All RH: 1987 Dioxin	0.001	1.29 (1.10,1.51)	Low: Medium: High:	9.6% 20.2% 24.9%	(a)
Composite Diabetes Indicator (pre-2002 AFHS diabetes definition) (18-5)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.010	1.34 (1.07,1.68)	Low: Medium: High:	22.1% 27.5% 27.0%	(b)
	4	All RH: 1987 Dioxin	0.001	1.27 (1.09,1.47)	Low: Medium: High:	12.3% 22.1% 27.6%	(a)
Diabetic Control (2002 AFHS diabetes definition) (18-6)	2	RH (1987 dioxin >10 ppt): Initial Dioxin – Requiring Insulin vs. Nondiabetic	<0.001	2.78 (1.61,4.82)	Low: Medium: High:	0.7% 2.1% 7.1%	(b)
	3	High RH vs. C - Requiring Insulin vs. Nondiabetic	0.016	2.66 (1.20,5.87)	RH: C:	5.6% 2.5%	(c)

Table H-10. *Summary of Results from Significant Adjusted Analyses in the Endocrinology Assessment (Continued)*

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Diabetic Control (2002 AFHS diabetes definition) (18-6) (continued)	4	All RH: 1987 Dioxin – Oral Hypoglycemics vs. Nondiabetic	0.006	1.32 (1.08,1.60)	Low: 3.9% Medium: 11.2% High: 14.0%	(a)
	4	All RH: 1987 Dioxin – Requiring Insulin vs. Nondiabetic	0.021	1.53 (1.07,2.19)	Low: 1.9% Medium: 1.2% High: 5.1%	(a)
Diabetic Control (pre-2002 AFHS diabetes definition) (18-7)	1	RH vs. C, Enlisted Groundcrew: No Treatment vs. Nondiabetic	0.037	0.51 (0.27,0.96)	RH: 4.2% C: 7.8%	(d)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin – Requiring Insulin vs. Nondiabetic	<0.001	2.90 (1.68,5.01)	Low: 0.7% Medium: 2.1% High: 7.1%	(b)
	3	High RH vs. C - Requiring Insulin vs. Nondiabetic	0.017	2.64 (1.19,5.83)	RH: 5.6% C: 2.5%	(c)
	4	All RH: 1987 Dioxin – Oral Hypoglycemics vs. Nondiabetic	0.005	1.32 (1.09,1.61)	Low: 3.9% Medium: 11.2% High: 14.0%	(a)
	4	All RH: 1987 Dioxin – Requiring Insulin vs. Nondiabetic	0.019	1.54 (1.07,2.21)	Low: 1.9% Medium: 1.2% High: 5.1%	(a)
Time to Diabetes Onset (2002 AFHS diabetes definition) (18-8)[a]	3	Background RH vs. C	0.030	0.69 (0.49,0.96)	RH: 33.17 years C: 28.41 years	(e)
	4	All RH: 1987 Dioxin	<0.001	1.28 (1.12,1.46)	Low: 34.42 years Medium: 26.75 years High: 23.67 years	(f)
Time to Diabetes Onset (pre-2002 AFHS diabetes definition) (18-9)[a]	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.033	1.21 (1.02,1.45)	Low: 25.75 years Medium: 25.91 years High: 21.58 years	(g)
	3	Background RH vs. C	0.030	0.71 (0.52,0.97)	RH: 33.08 years C: 28.41 years	(e)
	4	All RH: 1987 Dioxin	<0.001	1.26 (1.12,1.43)	Low: 33.50 years Medium: 26.75 years High: 23.67 years	(f)

Table H-10. Summary of Results from Significant Adjusted Analyses in the Endocrinology Assessment (Continued)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
TSH (18-12)	1	RH vs. C, All	0.024	0.096	RH: 1.653 µIU/mL C: 1.557 µIU/mL	(h)
	1	RH vs. C, Officer	0.009	0.189	RH: 1.778 µIU/mL C: 1.589 µIU/mL	(h)
	3	Background RH vs. C	0.036	0.122	RH: 1.682 µIU/mL C: 1.560 µIU/mL	(i)
Free T_4 (18-14)[b]	1	RH vs. C, Enlisted Flyer	0.002	0.061	RH: 1.115 ng/dL C: 1.054 ng/dL	(h)
Free T_4 (18-15)	1	RH vs. C, Enlisted Flyer	0.026	0.37 (0.15,0.89)	RH: 5.6% C: 13.8%	(d)
2-hour Postprandial Glucose (18-19)	1	RH vs. C, Enlisted Groundcrew	0.006	-7.4	RH: 107.4 mg/dL C: 114.8 mg/dL	(h)
2-hour Postprandial Urinary Glucose (18-21)	1	RH vs. C, Officer	0.050	1.48 (1.00,2.20)	RH: 23.6% C: 17.7%	(d)
	4	All RH: 1987 Dioxin	0.040	0.87 (0.76,0.99)	Low: 27.9% Medium: 25.5% High: 28.3%	(a)
Fasting Insulin (18-22)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.014	0.056 (0.023)	Low: 11.84 µIU/mL Medium: 11.86 µIU/mL High: 13.01 µIU/mL	(j)
Fasting Insulin (18-23)	2	RH (1987 dioxin >10 ppt): Initial Dioxin – Abnormal High vs. Normal	0.006	1.54 (1.13,2.09)	Low: 6.4% Medium: 9.9% High: 13.5%	(b)
2-hour Postprandial Insulin (18-24)	1	RH vs. C, Enlisted Groundcrew	0.033	-7.64	RH: 61.83 µIU/mL C: 69.47 µIU/mL	(h)
2-hour Postprandial Insulin (18-25)	1	RH vs. C, Enlisted Groundcrew – Abnormal High vs. Normal	0.043	0.70 (0.50,0.99)	RH: 49.1% C: 56.2%	(d)
Hemoglobin A1c (18-27)	4	All RH: 1987 Dioxin	0.031	1.35 (1.01,1.80)	Low: 48.0% Medium: 62.0% High: 73.4%	(a)
C-peptide (18-28)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.017	-0.091 (0.038)	Low: 3.69 ng/mL Medium: 4.17 ng/mL High: 2.88 ng/mL	(j)
Free Testosterone (18-36)	1	RH vs. C, Officer	0.039	1.87 (1.03,3.39)	RH: 9.2% C: 5.0%	(d)
LH (18-39)	1	RH vs. C, Officer	0.040	0.40	RH: 4.49 mIU/mL C: 4.09 mIU/mL	(h)
	3	Low RH vs. C	0.015	0.51	RH: 4.81 mIU/mL C: 4.30 mIU/mL	(i)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

(b): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal was presented for each of three initial dioxin categories.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(e): Continuous variable: adjusted hazard ratio and 95% confidence interval were presented; 10th percentile of distribution of time to onset of diabetes was presented for each dioxin category in contrast.

(f): Continuous variable: adjusted hazard ratio and 95% confidence interval were presented for a twofold increase in 1987 dioxin; 10th percentile of distribution of time to onset of diabetes was presented for each of three 1987 dioxin categories.

(g): Continuous variable: adjusted hazard ratio and 95% confidence interval were presented for a twofold increase in initial dioxin; 10th percentile of distribution of time to onset of diabetes was presented for each of three initial dioxin categories.

(h): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each exposure group in contrast.

(i): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each dioxin category in contrast.

(j): Continuous variable: slope and standard error were presented and were based on natural logarithm of dependent variable versus $\log_2$ (initial dioxin); adjusted means were presented for each of three initial dioxin categories.

[a]A smaller group mean or decreasing mean time to onset values as dioxin increased was considered adverse for this variable.

[b]A positive difference in means (Comparison mean less than Ranch Hand mean) was considered adverse to Comparisons for this variable.

Note: RH = Ranch Hand.
         C = Comparison.

   Model 2:   Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt).

   Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
               Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
               High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

   Model 4:   Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt (Ranch Hands only).

Table H-11. Summary of Results from Significant Adjusted Analyses in the Immunology Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
CD20+ Cells (B Cells) (19-8)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.016	0.102 (0.042)	Low: 187.2 cells/mm^3 Medium: 263.8 cells/mm^3 High: 257.7 cells/mm^3	(a)
IgM (19-13)	1	RH vs. C: Enlisted Flyer	0.031	-13.82	RH: 80.01 mg/dL C: 93.83 mg/dL	(b)
Lupus Panel: ANA Test (19-14)	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.035	1.28 (1.02,1.61)	Low: 19.5% Medium: 11.7% High: 27.8%	(c)

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Lupus Panel: MSK Smooth Muscle Antibody (19-16)	1	RH vs. C, Officer	0.045	5.27 (1.04,26.82)	RH: 2.2% C: 0.5%	(d)
	3	Background RH vs. C	0.021	3.91 (1.23,12.42)	RH: 1.9% C: 0.7%	(e)
	4	All RH: 1987 Dioxin	0.013	0.47 (0.26,0.85)	Low: 2.5% Medium: 0.4% High: 0.9%	(f)
Lupus Panel: Rheumatoid Factor (19-19)	1	RH vs. C, Officer	0.028	1.55 (1.05,2.28)	RH: 22.5% C: 16.1%	(d)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin	<0.001	0.61 (0.47,0.78)	Low: 30.9% Medium: 28.1% High: 15.1%	(c)
	3	Low RH vs. C	0.001	1.81 (1.28,2.57)	RH: 32.1% C: 20.2%	(e)
	4	All RH: 1987 Dioxin	0.042	0.87 (0.77,1.00)	Low: 21.9% Medium: 28.1% High: 21.9%	(f)

(a): Continuous variable: slope and standard error were presented and were based on natural logarithm of dependent variable versus $\log_2$ (initial dioxin); adjusted means were presented for each of three initial dioxin categories.

(b): Continuous variable: difference of adjusted means was presented; confidence interval was not presented because analysis was not performed on original scale; adjusted means were presented for each exposure group in contrast.

(c): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal was presented for each of three initial dioxin categories.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(e): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each dioxin category in contrast.

(f): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in 1987 dioxin; percent abnormal was presented for each of three 1987 dioxin categories.

Note: RH = Ranch Hand.
       C = Comparison.

Model 2: Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt. (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt)

Model 3: Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
          Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
          High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

Model 4: Low = ≤7.8 ppt; Medium = >7.8–19.2 ppt; High = >19.2 ppt. (Ranch Hands only)

Table H-12. Summary of Results from Significant Adjusted Analyses in the Pulmonary Assessment

Dependent Variable (Table Reference)	Model	Contrast or Description	p-Value	Analysis Statistics	Adjusted Mean or Percent Abnormal	Note
Pneumonia (20-5)	1	RH vs. C, Enlisted Flyer	0.046	1.94 (1.01,3.72)	RH: 19.7% C: 11.4%	(a)
FVC (20-8)[a]	3	Low RH vs. C	0.031	-2.52 (-4.81,-0.23)	RH: 93.22 percent C: 95.74 percent	(b)
Ratio of Observed FEV_1 to Observed FVC (20-12)[b]	2	RH (1987 dioxin >10 ppt): Initial Dioxin	0.039	-0.023 (0.011)	Low: 0.729 Medium: 0.740 High: 0.752	(c)
Obstructive Abnormality (20-14)	1	RH vs. C, Enlisted Flyer – mild vs. none	0.046	0.59 (0.35,0.99)	RH: 34.1% C: 43.1%	(a)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin – moderate vs. none	0.023	0.64 (0.43,0.94)	Low: 11.7% Medium: 8.6% High: 2.9%	(d)
	2	RH (1987 dioxin >10 ppt): Initial Dioxin – severe vs. none	0.036	0.44 (0.20,0.95)	Low: 4.4% Medium: 4.3% High: 0.0%	(d)

(a): Discrete variable: adjusted relative risk and 95% confidence interval were presented; percent abnormal was presented for each exposure group in contrast.

(b): Continuous variable: difference of adjusted means and 95% confidence interval were presented; adjusted means were presented for each dioxin category in contrast.

(c): Continuous variable: slope and standard error were presented and were based on natural logarithm of 1.0 - dependent variable) versus $\log_2$ (initial dioxin); adjusted means were presented for each of three initial dioxin categories.

(d): Discrete variable: adjusted relative risk and 95% confidence interval were presented for a twofold increase in initial dioxin; percent abnormal was presented for each of three initial dioxin categories.

[a]A smaller group mean was considered adverse for this variable.

[b]A positive slope was considered adverse for this variable; a negative slope implies an increase in the ratio because of the data transformation used.

Note: RH = Ranch Hand.
         C = Comparison.

Model 2:   Low = 32–79 ppt; Medium = >79–199 ppt; High = >199 ppt (Ranch Hands who had a 1987 dioxin measurement greater than 10 ppt).

Model 3:   Background (Ranch Hand): 1987 dioxin ≤ 10 ppt.
           Low (Ranch Hand): 1987 dioxin > 10 ppt, 10 ppt < initial dioxin ≤ 118 ppt.
           High (Ranch Hand): 1987 dioxin > 10 ppt, initial dioxin > 118 ppt.

APPENDIX I

APPENDIX I. ABBREVIATIONS AND ACRONYMS

A	adjusted analysis
ACE	angiotensin-converting enzyme
ADA	American Diabetes Association
AFHS	Air Force Health Study
Ah	aryl hydrocarbon
AIDS	acquired immunodeficiency syndrome
ALT	alanine aminotransferase
ANA	antinuclear antibody
APP	active pedal plantarflexion
AST	aspartate aminotransferase
ATS	American Thoracic Society
BUN	blood urea nitrogen
C	Comparison(s)
C	continuous analysis
CAPI	computer-assisted personal interviewing
CAT	computed axial tomography
CBC	complete blood count
CD	clusters of differentiation
C/D	continuous and discrete analyses for dependent variables; appropriate form for analysis (either continuous or discrete) for covariates
CDC	Centers for Disease Control and Prevention
CI	Cornell Index
C.I.	confidence interval
CMI	Cornell Medical Index
CNS	central nervous system
COPD	chronic obstructive pulmonary disease
COV	covariate
CS	chi-square contingency table analysis (continuity-adjusted)
D	discrete analysis
DEP	dependent variable
DNA	deoxyribonucleic acid

ECG   electrocardiograph

ESR   erythrocyte sedimentation rate

EXC   exclusion

FC   fully compliant at baseline examination

FEFmax   forced expiratory flow maximum

FEV_1 forced expiratory volume in 1 second

FSH   follicle-stimulating hormone

FTA-ABS   fluorescent treponemal antibody absorption

FTI   free thyroxine index

FVC   forced vital capacity

G   good (dioxin) result

GADA   glutamic acid decarboxylase antibodies

GFR   glomerular filtration rate

GGT   gamma glutamyltransferase

GLM   general linear models analysis

GND   good (dioxin) result, but below the limit of detection

GnRH   gonadotropin-releasing hormone

GNQ   good (dioxin) result, but below the limit of quantitation

GSH   (reduced) glutathione

GSI   global severity index

HBsAg   hepatitis B surface antigen

HDL   high-density lipoprotein

HIV   human immunodeficiency virus

HLA-DR   human leukocyte antigen-DR

HPF   high-powered field

HRB   Halstead-Reitan Neuropsychological Test Battery

IARC   International Agency for Research on Cancer

ICD-9-CM   International Classification of Diseases, 9th Revision, Clinical Modification

Ig   immunoglobulins

IL   Interleukin

IOM   Institute of Medicine

IQ   intelligence quotient

IRB   Institutional Review Board

K/DOQI   Kidney Disease Outcomes Quality Initiative

LAB   2002 laboratory results

LBBB   left bundle branch block

LDH   lactate dehydrogenase

LH   luteinizing hormone

LR   logistic regression analysis

MCH   mean corpuscular hemoglobin

MCHC   mean corpuscular hemoglobin concentration

MCMI   Millon Clinical Multiaxial Inventory

MCV   mean corpuscular volume

MIL   Air Force military records

MLC   mixed lymphocyte culture

MMPI   Minnesota Multiphasic Personality Inventory

MRI   magnetic resonance imaging

MR-V   medical records (verified)

MSK   mouse stomach kidney

NIOSH   National Institute for Occupational Safety and Health

NORC   National Opinion Research Center

NR   no (dioxin) result

NS or ns   not significant ($p > 0.05$)

OR   odds ratio

OMR   optical mark reading

PC   partially compliant at baseline examination

PCT   porphyria cutanea tarda

PE   physical examination

PH   proportional hazards analysis

PHA   phytohemagglutinin

ppq   parts per quadrillion

ppt   parts per trillion

PR   polytomous logistic regression analysis

PSA   prostate-specific antigen

PSDI   positive symptom distress index

PST	positive symptom total
PTSD	post-traumatic stress disorder
QA	quality assurance
QC	quality control
QRC	Quality Review Committee
Q-SR	AFHS health questionnaires (self-reported)
R	refusal at baseline examination
R^2	coefficient of determination
RBBB	right bundle branch block
RBC	red blood cell
RH	Ranch Hand(s)
RR	relative risk
RVN	Republic of Vietnam
SAIC	Science Applications International Corporation
SCL-90-R	Symptom Checklist-90-Revised
SEA	Southeast Asia
SEER	Surveillance, Epidemiology, and End Results
SHBG	sex hormone-binding globulin
T_3	triiodothyronine
T_4	thyroxine
TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin (or dioxin)
TLC	total lymphocyte count
TSH	thyroid-stimulating hormone
TT	two-sample t-test
U	unadjusted analysis
UNL	unlocatable at baseline examination
USAF	United States Air Force
VDRL	venereal disease research laboratory

WAIS   Wechsler Adult Intelligence Scale

WBC   white blood cell

WMS   Wechsler Memory Scale

WMS-R   Wechsler Memory Scale-Revised